JOURNAL OF THE

American Geriatrics Society

Official Journal of the American Geriatrics Society

Volume IX *December, 1961* Number 12

FATIGUE: A CASE HISTORY*

D. B. DILL, PH.D.

Department of Anatomy and Physiology, Indiana University, Bloomington, Indiana

So many phenomena have been described as manifestations of fatigue that the door is wide open for a panel discussion of the topic, "Fatigue." Knowing the interests of my fellow panellists, we may expect their discussions to be related to physical activity, to physical fitness and to the factors that limit the capacity for work. Much of my presentation constitutes a partial case history, the case being myself. The facts accumulated over nearly thirty-five years make up a "physiologic" history rather than the usual medical history. The responses of the cardiovascular system to exercise of all intensities will be described. We have learned something from this history about the changes that occur with aging. Further studies of this type may shed some light on how these changes can be slowed down or delayed.

RESPONSE OF THE CARDIOVASCULAR SYSTEM TO EXERCISE

In 1927 Bock and associates (including the author) (1) compared the performances of 4 subjects when they were operating the bicycle ergometer. Oxygen consumption ranged from baseline (sitting at rest) values to more than 2 liters per minute. The apparatus and methods were virtually the same as those in use today—the simple bicycle ergometer with a fly wheel, brake band and varying load; the Tissot type gasometer; and the Haldane apparatus. We used the indirect Fick procedure for estimating cardiac output, and derived from these values and the heart rate the stroke volumes. A few months ago I had the pleasure of hearing a paper on stroke volume in athletes and non-athletes presented by Dr. Yang Wang of the Mayo clinic. By cardiac catheterization and applying the direct procedure for cardiac output he derived stroke volumes that checked closely with ours of thirty-four years ago. Athletes had stroke volumes greater by 50 per cent than those of non-athletes for a given grade of work. All showed an increase of 50 per cent or more above the values observed when the subjects were sitting at rest. At Indiana University Bailie and associates (2) demonstrated in trained dogs that as the metabolic rate is increased, the stroke volume increases. From standing at rest to a run up-grade on the treadmill that required a fifteen-fold consumption of oxygen, the stroke volume increased 80

* Presented at the 18th Annual Meeting of the American Geriatrics Society, New York, N.Y., June 22-24, 1961.

per cent. We have not conducted any systematic study of the cardiac output and stroke volume during exercise as related to age, but Wang's report appears to validate the indirect Fick procedure we used thirty-four years ago and encourages us to apply the indirect Fick procedure to our current research on aging.

CASE HISTORY—EFFECT OF AGING ON HEART RATE AND OXYGEN CONSUMPTION DURING EXERCISE

Dill (3) reported that his maximal heart rate in exercise had declined from 172 to 162 from 1928 to 1941. This record was extended by Dill, Horvath and Craig (4), and a maximal heart rate of 160 was recorded in 1957 at age 66. Since then, additional studies have been performed. The results of 2 all-out experiments on the ergometer are shown in Figure 1. My present maximal heart rate during exercise is 150. It is interesting that in each of these 2 experiments, the first in 1932 and the second in 1961, the heart rate increased to 130 during the first minute; after that the rates diverged. In 1961 the oxygen consumption reached a peak value of 1.96 liters per minute during the sixth and seventh minutes, when exhaustion ended the experiment. In 1932, exhaustion came at the end of fifteen minutes, with a peak oxygen consumption of 2.75 liters per minute.

As an aside, these values for maximal oxygen intake do not apply to running on the treadmill. In 1932 my maximum on the treadmill (3.34 liters per minute) was 22 per cent greater than on the ergometer. In 1961 the treadmill value (2.30 liters per minute) was 11 per cent greater than the ergometer value.

A great many submaximal studies carried out on the bicycle ergometer in

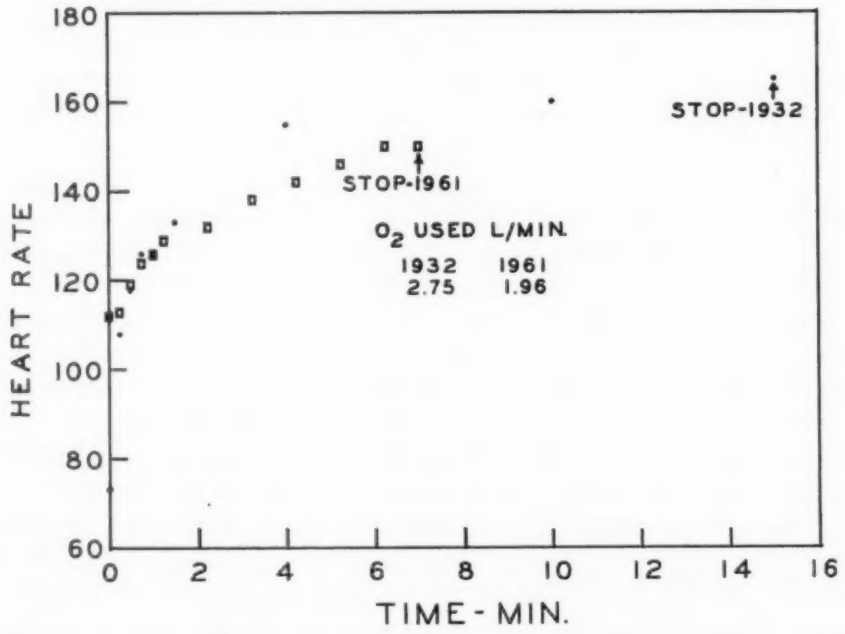

FIG. 1. Heart rate of Subject DBD during exhausting work on the bicycle ergometer. The performance in 1961 is contrasted with that in 1932.

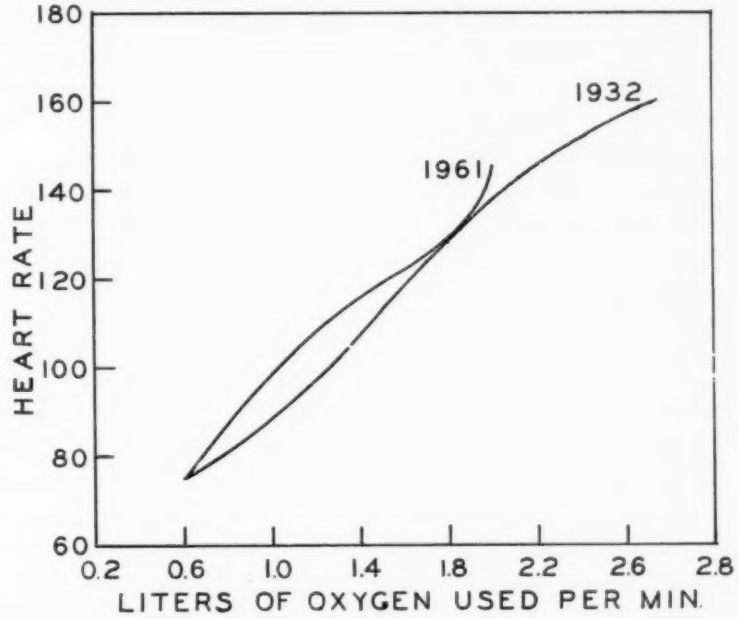

FIG. 2. Heart rate of Subject DBD during various grades of work. Observations made in 1961 are compared with those of 1932.

1931 and 1932 were repeated in 1961. The heart rates under temperate conditions are compared in Figure 2. In these curves every point represents one or more experiments. In 1961 the experiments were terminated at ten minutes; the heart rate during the tenth minute was counted from the cardiotachometer record. In 1932 the counts used in plotting were made in the tenth minute, but work commonly lasted for twenty minutes. The rates generally were lower in 1961, particularly for the intermediate grades of work. As exhaustion was approached, the pattern was quite different. In 1961 with an increase in metabolic rate from 1.9 to 2.0 liters per minute (the maximum in this form of exercise), the heart rate increased from 135 to 150, its peak value. There was no such sudden rise in 1932. As shown in Figure 1, in the all-out experiment the heart rate was 160 in the tenth minute and then rose to 165 after five more minutes of work.

BLOOD PRESSURE TESTS

A major role in the adjustment to the metabolic demands of exercise is played by elevation of the systolic blood pressure. Many records of blood pressure in exercise were published in papers from the Harvard Fatigue Laboratory, and still more were unpublished. Bock *et al.* (1928) published some observations on 3 subjects exercising on the ergometer. In the athlete, De Mar, the systolic pressure did not increase greatly until the oxygen consumption reached 2 liters per minute. Particular note was taken of Subject A. F., a physician at that time 35 years old, whose height was 180 cm. and weight 68 Kg. For some reason he had not been permitted to take severe physical exercise since the age of 14. At oxygen

consumptions of 2.05 to 2.30 liters per minute, his blood pressure readings increased from 140/80 mm. Hg at rest to 230/90 after two minutes of work and to 260/90 after fourteen minutes of work. This man today is in good health. He retired recently after a successful career in physiology and at age 69, in retirement, he enjoys skiing and other outdoor sports.

We were unable to obtain reliable values for blood pressure while running or even walking on the treadmill and had to be satisfied with observations during recovery. These do not give a fair picture of the situation in exercise, as illustrated by the following observations by Bock *et al.* (1) on subjects during recovery from exercise on the ergometer:

	Subject DeM	Subject AF	Subject CVC
B.P. during work	145/85	260/90	165/90
B.P. after 15 seconds of recovery	120/80	200/?	135/65

In recent years Balke has developed a treadmill test of great usefulness. Its application in assessing the fitness of Air Force personnel has been described recently by Balke and Ware (5). The treadmill speed is constant at 90 meters per minute or 3.36 miles per hour. At first the treadmill is horizontal; at the end of each minute its angle is raised 1 per cent. It is stopped when the heart rate reaches 180 or when the subject is exhausted, whichever happens first. Balke and Ware found it possible to observe the blood pressure during this test. The cuff is held in place with elastic tape and is inflated once a minute; the diaphragm of the apparatus is secured in place over the brachial artery and the tubes are not allowed to swing against the body or treadmill supports. The systolic pressure is read during the first fifteen seconds of each minute; as the pressure drops the the pulse is counted for fifteen seconds, after which the diastolic pressure is read. During a recent visit Dr. Balke demonstrated his technique on Dr. Robinson as subject. At the same time observations were made on the pressure in the radial artery of the other arm, using an indwelling catheter and strain gauge. The two techniques checked satisfactorily. Accordingly we are now satisfied that blood pressures can be read while the subject is walking on the treadmill, even when the grade is great enough to demand the maximal oxygen intake.

CASE HISTORY—HEART RATE, OXYGEN CONSUMPTION AND BLOOD PRESSURE DURING EXERCISE (4-YEAR PERIOD)

I have been a subject in the Balke test on four occasions beginning in 1957. Since I cannot attain a heart rate of 180, the end-point has been exhaustion. The records of heart rates for 1957 to 1959 are shown in Figure 3. A significantly higher level of heart rate was maintained throughout in 1957, when exhaustion ended the work at fifteen minutes with a final heart rate of 160. During the next year, dieting brought my weight down from 80.5 to 72 Kg. Probably largely due to that reduction in weight, my limit was seventeen minutes in 1958 and sixteen minutes in 1959. The heart rates up to the fifteenth minute were lower by from 10 to 20 beats in the latter two years than in 1957. In the extra two minutes of

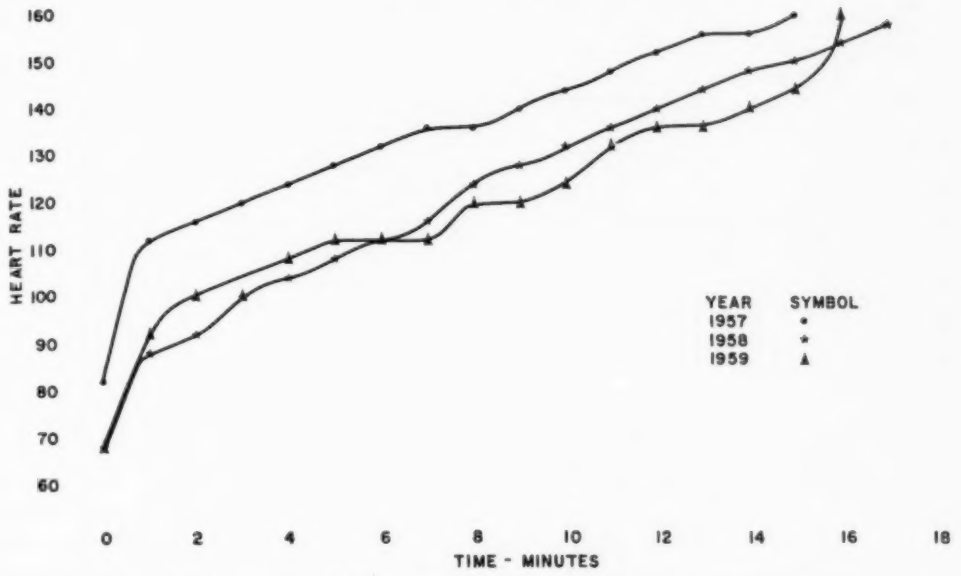

FIG. 3. Heart rate of Subject DBD in the Balke test, 1957 to 1959

work in 1958 there was a gradual rise in the last two minutes from 150 to 160, whereas in 1959 there was a sudden rise during the last minute from 145 to 160. Early in June 1961, the Balke test was repeated, except that there were no observations on blood pressure and the heart rate was recorded on the cardiotachometer. My weight was about the same as in 1958 and 1959; I was able to walk for sixteen minutes, the same length of time as in 1959. However, my maximal heart rate (150) was less and my oxygen consumption (2.3 liters per minute) was in contrast with 2.75 liters in 1957, 2.6 liters in 1958 and 2.5 liters in 1959. Oxygen was used at a constant rate in the last three minutes—2.31, 2.30 and 2.30 liters per minute. Evidently, in this form of exercise, my maximal attainable oxygen intake is 2.3 liters per minute. Since the increment in oxygen consumption for each per cent of grade up to 14 per cent was 0.12 liter per minute, an increase in oxygen debt was required for the extra climbing in the last two minutes—0.12 liter in the fourteenth minute and 0.24 liter in the fifteenth minute, a total of 0.36 liter. The blood lactic acid concentration at the end was 34 mg. per 100 ml. This level of lactic acid corresponds to a lactacid oxygen debt of about 2 liters. Further studies are required to measure the total oxygen debt and its components and to determine at what stage lactic acid begins to accumulate.

The records of blood pressure in the Balke tests of 1957 to 1959 are shown in Figure 4. The highest levels for both systolic and diastolic pressures occurred in 1957. In 1958 and 1959 the responses were nearly identical throughout. The systolic pressure rose gradually from about 135 mm. Hg at three minutes to about 150 mm. at fifteen minutes. From this point there was a rapid rise to about 175 mm. At the same time the diastolic pressure was unchanged until the fourteenth minute, when a rise occurred.

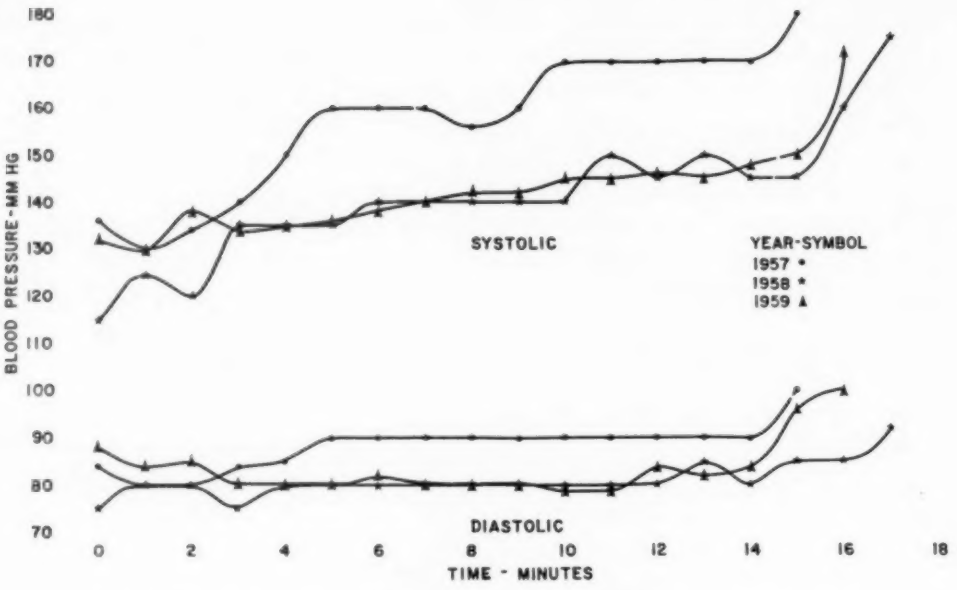

FIG. 4. Blood pressures of Subject DBD in the Balke test, 1957 to 1959

COMMENT

No generalizations can be made about these observations on cardiovascular responses to exercise. The data are presented on the grounds that you are interested in such case histories. Many of these case histories must be written before the stage of generalization is reached. Dr. Robinson and I plan to bring to our laboratory as many as possible of those who were subjects in our experiments twenty to thirty years ago. In another year we should have a respectable body of data which may be useful in establishing procedures for evaluating physiologic age. The need for this was emphasized recently by Mohler (6). Perhaps, on the basis of present knowledge, my fellow panellists may be willing to make some assertions about ways and means for slowing down the aging process.

Before anyone asks, "What do your experiments have to do with fatigue?" let me assert that they all lead to fatigue, some to profound fatigue. All have been followed by prompt recovery with no unpleasant after-effects. As stated a few years ago (7), "Fatigue is to be desired rather than feared. Life without stress is uninteresting and unhealthy. The man is fortunate whose work tires him, gives him a good appetite and promotes a good night's sleep."

SUMMARY

An account is given of the author's cardiovascular responses to exercise today as compared with twenty to thirty-four years ago. This "case history" is a pattern for other planned studies. The experiments included exhausting work on the treadmill and on the bicycle ergometer. The responses to each form of exercise were determined in relation to age and the fatigue engendered.

Acknowledgment

I am indebted to Dr. Bruno Balke and his associates at the Aerospace Medical Center for part of the data reported here. Dr. Balke's present address is Civil Aeromedical Research Institute, Federal Aviation Agency, Oklahoma City, Oklahoma. I am also indebted to Dr. Sid Robinson and the staff of this Department.

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CHANGING PATTERNS OF BACTERIAL INFECTION*

GEORGE EASTMAN, M.D.†

Pleasant Hills, Pittsburgh, Pennsylvania

Because of the rapid accumulation of information in both the clinical and preclinical medical sciences, some medical educators have redefined the type of knowledge and training needed for the successful practice of current scientific medicine. They believe, with considerable justification, that the future of the physician will be found in his acceptance of the role of human biologist, with an understanding of the total biology of the species both in health and disease.

This concept is of obvious value in the study of the various degenerative diseases, and the chronic diseases of the aging process. In the field of infectious diseases, there is also a place for an over-all biologic viewpoint. One of the divisions of biology which is of particular interest to the student of bacterial infection is ecology. Ecology, can be defined as the study of the inter-relationships and interdependence of the various living species which inhabit a given environment.

The basic assumption which underlies the study of ecology is that profound dependences exist between the various species which live side by side, and that disturbances affecting one of the species can produce major effects on its neighbors, sometimes by way of a long and complicated cause-and-event chain.

ECOLOGIC CHANGES

Examples of this type of sequence can be seen in the diminution in numbers of, and sometimes extinction of a species of wild animal, not usually as a result of deaths from hunting, but as a result of loss of necessary food or breeding grounds caused by the encroachment of civilization on a previously wild environment.

Ecologic changes can also result from the introduction of a new species into an area where it previously had not existed. The sparrow and the starling in the United States, the rabbit in Australia, and the mynah bird in Polynesia are all species which have taken over a large proportion of the available food supply and hence have assumed important numerical status in environments to which they previously were not indigenous. This sort of "overgrowth" is explained not only by the availability of food in the new area, but also by the absence of the natural controls such as disease and predators.

On the microscopic level, the deliberate introduction of rabbit myxoma virus by man into Europe and into Australia (to control rabbit overgrowth) found the host species completely without natural defenses and therefore the disease spread rapidly, widely, and nearly but not completely annihilated the rabbit. Resistant strains of rabbits appeared in both ranges, so that it appears likely that the European hare will not become extinct.

The changes in ecologic relationships brought about by natural processes are usually slow and relatively inapparent. The processes of random mutation, fol-

* From a Basic Science Seminar, McKeesport Hospital, McKeesport, Pa.

† *Address*: 102 Old Clairton Road, Pleasant Hills, Pittsburgh 36, Pennsylvania.

lowed by natural selection of changes having additional survival value, are multi-generation events which, dependent upon the generation interval, may take millenia to make their influence noticeable. On the other hand the interventions imposed on natural flora and fauna by man are abrupt, sometimes violent, and occasionally catastrophic to the species involved.

The relationships which have existed for many past eons between Homo sapiens and his saprophytic and pathogenic guest micro-organisms have recently been violently disturbed, and it is the description of these changes and their consequences which is the concern of the new bacteriology now being evolved.

THE NEW BACTERIOLOGY

As recently as a single generation ago bacteriology, although not having reached a dead-end, appeared to have achieved a stable position from which further detailed work on the fundamentals of bacterial biochemistry and immunology might be explored without considering changes in the established patterns of the common pathogens of man. The various types of Gram-positive cocci and Gram-negative rods occupied the central position in classifications and the remaining important bacterial species were studied as peripheral groups differing from the underlying established basic pattern.

The violent disturbance which ended this now obviously naïve viewpoint was the introduction of antibiotics and chemotherapeutic agents. Man's influence on the patterns of bacterial infection has produced a situation never previously existent in the history of the host and parasite species involved. Exploration of this change and the manner in which it came about is the primary purpose of this seminar.

RESISTANCE TO ANTIBIOTICS

When a patient is given an antibiotic for a particular bacterial infection, one of three events occurs: 1) the infection is nonresponsive, and no effect is made on the bacteria or the clinical status of the patient; or 2) the bacteria are sensitive, and the antibiotic is bacteriocidal, so that the organism is eradicated in that particular host at that specific time; or 3) the antibiotic in the dosage used is only bacteriostatic, so that a combination of its effect plus the natural defenses of the patient may overcome the infection. These are all individual situations involving the single patient.

Additional factors appear when one considers the effects on a number of patients with a certain bacterial infection treated with the same antibiotic.

Of primary interest is what appears to be the nearly inevitable development of antibiotic resistance by at least some pathogenic bacterial species. The rapidity of its development as well as the level of such resistance is related to the total amount of antibiotic used in a particular environment during a particular time period.

Types of resistance

Two types of antibiotic resistance have been described. When viewed from the bacterium's frame of reference, these can be called active and passive defenses.

The active type of bacterial resistance to antibiotics is exemplified by "hospital staphylococcus" (the specific phage types of coagulase-positive hemolytic Staphylococcus aureus). The organism has acquired the ability to produce a specific anti-antibiotic substance, a penicillinase. This type of resistance has produced a serious, widespread problem.

The more common type of antibiotic resistance is exemplified in situations such as tetracycline resistance. Here the organism has acquired the ability to exist and reproduce despite a concentration of the antibiotic sufficient to inhibit one or more essential metabolic steps in the metabolism and reproduction of a sensitive strain of the same bacteria, without elaborating a specific anti-antibiotic substance.

Basic mechanism

The basic mechanism of this type of antibiotic insensitivity may be explained in a general outline of the organic reaction pathways seen in all living organisms, as follows:

Substance A $\rightleftharpoons$ Intermediary metabolite B $\rightleftharpoons$ Intermediary metabolite C $\rightleftharpoons$ End-product D.

Each step in the reaction pathway is catalyzed by a specific enzyme with or without co-enzymes or essential electrolytes. If the end-product D is essential to the energy metabolism or to the protein or nucleic acid synthesis of a living cell, and if no alternative pathways for its production are available, then interference with any of the steps shown, by the inactivation of one of their catalysts, will lead to failure of the bacteria to survive and proliferate.

Even if alternative pathways exist, reproduction, with its generally higher requirements of protein, nucleic acids and energy, may be suspended. It is thought that the general method of action of the antibiotics (and also many other drugs) is one of influencing the cellular enzyme systems that catalyze vital cell synthetic or energy-producing reactions.

Genetic patterns

Changes in the genetic patterns of all animals, and hence changes in the structure of such protein enzymes, continually occur. However, because of the relatively small numbers of animals existent at any one time as compared to the number of bacteria co-existent, and because of the relatively much longer generation time, the mutations which cause these changes usually affect only a few individual humans or animals, and then usually affect them only in subtle biochemical ways that are difficult to detect.

On the other hand, because of the immense proliferative capabilities of unicellular organisms, multiple mutations frequently occur that produce organisms which differ from their forebears in various biochemical ways in nearly every generation. Thus in a patient who is the involuntary host of many millions of a species of pathogenic bacteria, there may exist at any time a few bacteria which are not affected in the same fashion by the attainable concentrations of antibiotics in the tissues as are the vast majority of their brothers. If this different

reactivity is capable of giving the bacteria possessing it a differential survival advantage, then the greatly accelerated processes of natural selection will insure that within a matter of a few hours or days, they will be the ancestors of all the organisms of that particular species found in that particular host.

Propagation to other hosts then is all that is required to establish firmly in the general population another strain of antibiotic-resistant organisms.

This entire phenomenon is thus capable of description and understanding in ecologic terms.

Action on cells

Some of the ultimate cellular action of antibiotics is known, and some remains in the realm of conjecture. The sulfonamides compete for the cellular enzymes with para-aminobenzoic acid, and since they successfully tie up these enzymes, the transformation of PABA to folic and folinic acid is blocked, thus in turn inhibiting the synthesis of methionine, serine and particularly thymine. This last compound, a progenitor of nucleic acid, is essential for the production of ribose nucleic acid (RNA) which is an integral constituent of chromatin reproductive reactions.

Penicillin has been described as having its effect by blocking the incorporation of a uridine nucleotide, an acetyl sugar and a polypeptide into the bacterial cell wall. It can readily be seen that so direct a mode of action, as opposed to the more indirect pathway described for the sulfonamides, provides an explanation for the bactericidal effect of penicillin in contrast to the mere bacteriostatic action of the sulfa compounds.

The actions of both the tetracyclines and chloramphenicol have been claimed to be similar in the inhibition of protein synthesis, but examination of their chemical structures shows so wide a degree of dissimilarity that it appears more reasonable to postulate different modes of action.

The presence of a nitro group in chloramphenicol (Chloromycetin) is unique in the known structure of antibiotics and may explain the apparent greater tendency of this substance to provoke hematologic disorders in susceptible patients.

THE WIDENING SPECTRUM OF PATHOGENS

The development of antibiotic resistance in the individual patient means that either his infection is cleared more slowly by natural immune processes, is cured by another antibiotic to which the organism is not resistant, or may not be cured and thus lead to death.

On the other hand, the influence of the use of antibiotics on the human species as a whole may be considerably more complex. Some infectious diseases can be almost totally controlled by these agents, whereas others in which the causative organisms become resistant more easily may show either increased or unchanged epidemiologic (total population) virulence. In addition, as a result of the suppression of what were previously the more common etiologic bacteria, a number of clinical entities are now associated with a much wider spectrum of possible bac-

terial agents; this must be considered in making the cultures necessary to establish the nature of the offending pathogen. Examples of this phenomenon of a widened spectrum of potential pathogens are particularly prominent in connection with the pneumonias, the various forms of endocarditis, and urinary-tract infections.

Pneumonia may be caused by such unexpected pathogens as Pyocyaneus, Proteus, Klebsiella-aerogenes, E. coli, the enterococci, and the Nisseriae. Endocarditic disorders show an even wider group of "exotic" pathogens such as Mima polymorpha, B. antitratum, Vibrio foetus, and Listeria monocytogenes.

The emergence of Aerobacter aerogenes, previously thought to be a saprophyte, to a prominent position in the etiology of urinary-tract infection has been well documented. A considerable number of such infections also are caused by Proteus and Pyocyaneus, both of which were previously thought to be only nuisance bacteria in the laboratory rather than the important pathogens they have become.

For nearly all of the foregoing organisms, one can trace the effect of ecologic alterations produced by the use of antibiotic and chemotherapeutic agents.

In addition to antibiotic resistance or change in pathogen pattern, is the appearance of new organisms and families of bacteria as possible etiologic agents in disease.

Included in this group are the Mimae, Vibrio foetus, Leptospirum, Spirrilium minus, Listeriae, the atypical Mycobacteriae, some of the rarer of the Salmonella group, and organisms like those causing pleuropneumonia.

Organisms of the tribe Mimae, particularly Mima polymorpha have evoked recent interest because of the similarity of their morphologic and staining characteristics to those of the Nisseriae. This probably accounts for reports on the existence of penicillin-resistant gonococci. These organisms also have been found in other infections including pneumonitis, subacute bacterial endocarditis, and conjunctivitis.

Vibrio foetus, an organism which can cause fever of "unknown origin," must be differentiated from the Leptospirae and the Spirillii, but the major importance lies in the fact that, though normally an animal pathogen capable of causing abortion in its usual hosts, it has also been implicated as a causative agent in human abortions otherwise unexplained.

The Salmonella group of organisms causes many enteric infections which do not follow the typical typhoid pattern and hence are not readily diagnosable without a high index of suspicion and a good bacteriologic laboratory. Modern food technology has provided conditions which are particularly likely to permit widespread dissemination of these organisms. The pre-preparation of foods involving their heating to temperatures in the bacterial incubation range, their preparation in large-scale amounts followed by their freezing to deep-freeze temperature ranges, and their wide commercial distribution and subsequent reheating for serving, all create ideal conditions for the production of Salmonella epidemics while increasing inordinately the difficulties in investigating such outbreaks.

The atypical Mycobacteria confuse and render more difficult the correlation between the findings by direct smear and those obtained by cultural and the animal inoculation methods in the diagnosis of tuberculosis. They also give rise to problems in the determination of their sensitivity to antibiotics, when they are present in mixed cultures.

The organisms of the pleuropneumonia-like (PPL) group have been proposed as etiologic agents for rheumatoid arthritis and Reiter's syndrome. These hypotheses have not been confirmed to date.

CONCLUSIONS

The use of antibiotics and chemotherapeutic agents was once jestingly proposed as sounding the death knell of the science of bacteriology by the simple process of total elimination of the objects of study. However, a profound change, not entirely expected, has been wrought in this field. As a result, bacteriology has become more complicated, more difficult and even more interesting.

CHARLATANS, INC.

NATHAN MASOR, M.D.*

Staten Island, New York

Organized medicine is ofttimes powerless in offering discernible relief to those who suffer from certain physical or emotional ailments, a situation that unhappily may contribute to the growth of cultism. Sometimes a word of encouragement, a smile, or even a white lie may be the few remaining therapeutic instruments for relief of suffering in a minority of cases. In such instances, the clergy may perhaps contribute to more beneficial results by administering to the human spirit.

Although the quack considers a person in any age group to be fair game, more often than not his most effective efforts are directed against the lonely, the troubled and the weak. The geriatric population statistically offers least resistance to his patronage, though he recognizes that no age has a monopoly on gullibility.

It is quite understandable, therefore, that when conventional orthodox methods of care, with or without spiritual help are insufficient to ease human suffering, some people will turn in despair to the army of modern voodoo practitioners, gadgeteers, faddists and medical con men for possible relief. What is less understandable is the fact that a large segment of the so-called normal intelligent population is always ready and willing to embrace the numerous charlatan methods.

Every culture and society since antiquity has witnessed its own brand of cultism as a protest against conventional methods in the healing arts. The shamus, witch doctor, crystal gazer and voodoo practitioner are perhaps more prevalent now than in the days of old. The techniques, dress and double-talk may differ in the various cults, but the common ingredient remains the same, namely, the attempt on the part of the healer (or whatever he may call himself) to dispense with natural law in favor of some extrasensory perception which can only be a function of the supernatural. Through such unique powers he believes he may clandestinely arrive at the ultimate truth of either past, present or future events.

CULTIST PRACTICES

In applying his remarkable talents to actual practice, various methods are used, depending upon the type of cult. Closest to enjoying respectability, through irresponsible references and identification with the Deity, are the so-called depth psychologists and faith healers. With both types, mysticism, unproven anachronisms, with liberal sprinklings of blessings from the Scriptures, are skillfully intermingled to support their own declared points of view. Thus far, the faith

* *Address*: 392 Forest Avenue, Staten Island 1, New York.

healer has remained relatively free from criticism, due to the immunity of his sacrosanct cloth. Acting alone or in concert with the depth psychologist, the faith healer may promise aid where none is possible, for theirs is the ultimate knowledge of the laws of the mind and body. For a price they will share their priceless secrets. They may be revealed in "healing clinics," in the pulpit and even in intimations over the radio, not to mention bizarre spiritual carnivals sometimes conducted as "seminars on the high seas." The only requirement for salvation at their hands is faith and money, predominantly the latter.

The depth psychologist is not too distantly removed from the crystal gazer, except that he is not a gadgeteer. His tools are intuition, insight and fantasy, which he uses to pry open the secrets that lie hidden in the depths of the psyche. He believes that the deliberate use of fantasy is an important means of gaining new empirical knowledge. Midst the ecstasy of learned ignorance, he then descends, along with the patient, into the lowest "tiers" of the mind by closing his eyes and entering a dream state. This near-trance method allows him to be creative by unearthing facts deeply recessed, he claims, and the emergent dreams (but not the snores) are of value in understanding symptoms. Although his language is mystical and is borrowed from the quacks of all times and all places, he operates in modern dress and setting and belongs to the new emergent charm school of modern charlatanism, wherein nothing that is said is really understood, yet it sounds so captivating. In reality, the depth psychologists and faith healers are psychologic and spiritual voyeurs who rejoice in the nakedness of the human soul and imagination.

It is noteworthy that many purveyors of cultist practices, whether through yoga, voodooism, spiritualism, depth psychology or telepathy, utilize hypnotism to some degree. This is resorted to, not as a form of accepted therapy in common use by medical men who are familiar with its ancillary aid in treatment, but as a sinister modality to remove the obstacles for faith, misplaced though it may be. A stern authoritarian voice, a darkened room, a monotonous repetition of sounds or voices, a series of colored lights playing upon a fixed object, and the use of incense, are some of the unconscious ruses of the quack. These are the persuasive props used in heightening suggestibility and reducing resistance. Charlatans also claim the power to effect regression of the individual to a previous existence in another age and with all due compensation to follow.

Probably the most inherent characteristic of those easily duped is their sensitivity. This quality of emotional lability is charged with all sorts of feelings, both pro and con. The gullible are bored with their occupations, surroundings and associations, and actively crave vicarious outlets for their inner restlessness. Theirs is the constant search for the thrill of experiencing the unknown, the forbidden or the unreachable. They are impatient and eager to speculate in search of so-called truths and secrets, through methods that the pure physical sciences never dare to embrace. To some, the thrill of the search is as great as the promise of an ultimate reward. Tales of the spirit world, ghosts, and visits from outer space are often accepted with the same degree of validity as are stock market reports in the newspapers. Such emotional bankruptcy among the gullible is

generally completely compatible with otherwise normal mental functioning, so that they do not as a rule stand out as queer persons.

The cultists well understand this sensitive, restless nature among their victims and will use every psychologic ruse to play upon such hypersensitivity, namely, flattery, reassurance, sympathy and, whenever necessary, even fear. Thus the gullible are swayed by appeals to emotion because somewhere along the line they have traded mature judgment for misinformed confusion.

Cultists often claim that they have the power to see their clients surrounded in different auras or colors of varying hues, sizes, shapes and intensity. These become telltale signs of the individual's past, present and future lives which they will hasten to interpret. Some charlatans claim to be able to "tune in on the wave lengths" of their clients, even though they reside at a distance. This unique power makes it most convenient for prospective clients to get a reading, though far removed from the mentalist, whenever travel is impossible. Inanimate objects belonging to a client may also be sent in for a "reading" made by virtue of mysterious waves imparted through close association with the owner. To this most pragmatic form of analysis, is given the name of psychometry. In any case, the underlying theme of each cult is the same, namely, the authoritarian power of the high priest to elicit the aid of the supernatural through extrasensory perception, in uncovering the secrets of the body, mind or soul as the individual case may require. Modern dress, the couch, the telephone, and the tape recorder are merely twentieth century implemental substitutes for witches' brew, voodoo dances and hex practices.

Numerous variations and gradations of the alleged mystical power of cultists exist, depending upon the timidity or audacity of the charlatan. When one considers that charlatanism breeds on the taste buds of those impatient people who hunger for quickie or miracle cures, one can understand how fertile is the medium of public ignorance.

Enthusiasm for the incredulous may even run amuck in the minds of the genius—even in those who should have been most qualified to denounce cultism. Thus, Dr. Sigmund Freud created an imposing system of infantile sexuality to explain and treat all the tribulations of the disturbed mind. His influence deeply invaded not only organized medicine, but also psychiatry, sociology and anthropology, to such extent that it will take many more years to unshackle the chains of captive medical minds from the intellectual slavery he imposed upon them. Is it any wonder that lay minds, not scientifically oriented, should seek refuge for their difficulties in the darkened alleys of cultism!

Cultists will vigorously defend any slur or allegation that may cast doubt on the legitimacy of their trade or the efficacy of their purported cures. Thoroughly lacking in any degree of conscience they will studiously sidetrack any discussion that may interfere with the logic of their own brand of legerdemain. Their writings will utilize timeworn clichés such as "within this frame of reference," and also half-truths, to impart precise impressions or background evidence for the rationale of their methods. They are masters of double-talk, of meaningless, though euphonic words, and phrases borrowed from the medical dictionary.

They embrace the scientist as their strange, unwilling bedfellow, and all too often the latter is powerless by law to protest against this type of seduction. At times, the cultists are so fanatical in their make-up and so effective is their social camouflage that an observer may well suspect the charlatan to have effectively hypnotized even himself to a state of belief in his own inordinate powers. There is little doubt that when this self-delusion occurs, the healer borders closely on the lunatic fringe of his profession and is then doubly dangerous. One must, therefore, not suppose that the haunted house, the witches' brew, visitations from outer space, and reincarnation are subjects merely for fireside chats on rainy days, or to serve as fill-in discussions whenever television programming is hopelessly dull. Ghosts dwelling in Long Island homes, witches disguised as beautiful show girls, talking animals who were once people, and inhabitants of other planets posing as automotive mechanics in Pennsylvania are constantly near us, if one would believe these experts of occult practices.

SPECIFIC INCIDENTS

Some time ago, an organization concerned with parapsychology circulated a questionnaire among physicians requesting information concerning any supernatural phenomena their patients may have displayed just prior to death. Obviously there were no phenomena in my case histories not explainable by natural law, and I stated so in my reply. Yet I was further asked to explain certain hallucinatory tendencies of the dying as possibly related to supernaturalism. Here was a bold attempt to enlist and influence the medical profession regarding occult phenomena. More repugnant was the disregard of the sanctity and true meaning of the process of dying. There is as yet no defense against these zealous eavesdroppers of human dignity other than the normal obligation to ignore them.

This writer might not have felt impelled to serve a warning to that segment of the population who are fair prey to the charlatan, were it not for being a recent witness to a séance wherein an attempt of the client to adhere to the irrational advice of the healer might have resulted in catastrophe. Against my advice, a female patient in her thirties took it upon herself to consult a mentalist in a search for relief for a painful condition of her fingers (Raynaud's disease). Previous consultation with medical specialists in vascular diseases left her passionately disillusioned with the medical profession. She read exhaustively the articles put out by cultist magazines, which led her to the offices of a mentalist whose motto was publicized as "The Invisible Bond is the Strongest." The brochure listed the mentalist's primary interests as "extrasensory perception, philosophy, comparative religions, science and scientific theories, psychology and parapsychology, the occult, flying saucers, metaphysics, brotherhood, psychic phenomena, re-incarnation and hypnosis." I accompanied her on this trip, not merely as an observer of sorcery practice, but as a measure to prevent harm.

The cultist answered all the requirements of a biblical, medieval and modern Aladdin. Among her publicized accomplishments were her alleged abilities while in a trance to predict accurately newspaper headlines a week hence, describe the

contents of sealed boxes to owners whom she didn't know, and to tell clients specific things about themselves and their homes. She also was able to hypnotize herself to previous existences in Persia in 1200 A.D., and again to Vienna in the middle 1820's. While in her hypnotic trance she could converse fluently in the German language and play the piano, neither being possible while conscious. She could also read x-ray plates accurately while in the hypnotic state, even though the plates might be far removed. These powers were only a part of the wonders in the magic grab bag of the sorceress we visited.

The library was replete with books on mysticism, magic, supernaturalism and the like. A long table contained recently published periodicals concerning the healing powers of the mentalist and the parapsychologist, religious mysticism, and journeys to distant planets. Articles on wave transmission from person to person, and person to object were similarly evident. The mentalist my patient consulted was a female, with all the attributes of a yogi, swami, witch doctor and telepathist rolled into one. She told me she was indeed proud of her powers, attested to by one of the finest Jungian psychologists of New York.

She then proceeded (for a fee of $25.00 to her patient, henceforth to be referred to as the "body") to attempt a "reading of the body" for purpose of diagnosis and suggestions for treatment. She refused to offer proof (as she promised she would on the telephone) of her unique powers, such as relating to me the contents of a letter in my pocket. Her husband explained that "we are unwilling to offer proof of our scientific prowess because we have already done so hundreds of times."

The female mentalist, on a command of "hocus pocus" by her husband to the effect that her soul could now leave her body, then proceeded to lie supine on the couch. She soon began jerking various muscles of her body spasmodically, preliminary to entering her trance state. Meanwhile the odor of incense began to permeate the air. During this state she was supposed to be oblivious to all outside impressions save the verbal questioning of her husband seated at the head of the couch. It was he who relayed the questions from the "body" to the mentalist for a reading.

It took approximately fifteen minutes for the cultist to enter the state of "samadhi" as designated by yoga—meaning her trance. During this interval I asked the assistant in the room whether he had ever gone through a similar reading. He replied that he underwent two readings, once for treatment of an emotional disorder and another time for a reading of his future. He briefly recounted his experiences with such satisfaction that he must have drooled several times. This reading took about thirty minutes, and words were used that have not as yet found their way into standard dictionaries. Medical terms were also tossed about with reckless abandon. The only two concrete gems of wisdom I could detect were that the "body" was severely anemic, so much so that her white cells outnumbered the red and needed correction, and that the remedy for the "body" resided in exercise, especially massage of her finger tips. With regard to the pronouncement of anemia, a laboratory examination the following day proved

her blood count to be perfectly normal. As for finger massage, the pain fortunately made it impossible for the client to follow the mentalist's suggestion.

It took fifteen minutes for the cultist to unwind from her state of "samadhi" on a signal from her husband, but less than a minute for the "body" and myself to draw a hasty retreat to the waiting automobile.

If the patient was confused in her judgment prior to this séance, she was utterly confounded during the trip home. She was intelligent enough to recognize the unorthodox methods of approach to her problem. However, hope springs eternal in the human breast, and strikingly so with the gullible. Just as there are good and bad physicians, she explained, there must also be bona fide and fake mentalists. Her search for the supernatural, therefore, continues, as it does with many thousands of misinformed people.

When the charlatan leads his blind patient over an obstacle course of ignorance, there is not even the sound of friendly voices to lead the way back to safety. Unless society recognizes this menace to human dignity through effective legislation, the divine powers of the Deity will continue to be mocked in the oblique pursuit of the unknown.

CONCLUSIONS

Charlatanism has many faces. They are all born in the midst of scientific ignorance, are cradled in the false hopes of suffering humanity, are strengthened by the impotence of the law, and are immortalized through organized medicine's tolerance of certain kindred unscientific psychic disciplines.

It should be the task of organized medicine, therefore, to turn its analysis first on itself, and determine what sanctuary it gives to strange systems of therapy that self-identify themselves as bedfellows of science.

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HOST-TUMOR ANTAGONISM. XX. THE INFLUENCE OF PREGNANCY ON TUMOR GROWTH*

LOUIS PELNER, M.D., F.A.C.A.†

Swedish Hospital, Brooklyn, N. Y.

STATEMENT OF THE PROBLEM

Single case reports abound in the periodical literature, both to show how serious cancer becomes when associated with pregnancy and alternatively that the prognosis is often much better than expected. The incidence of pregnancy co-existing with cancer is very low and has been estimated by various authorities to be 0.05 per cent. Way (1) noted 11 cases of cancer in a series covering approximately 19,000 deliveries—also an incidence of 0.05 per cent.

The literature is full of references to pregnancy co-existing with malignant disease, or following the treatment of cancer, but the majority of these articles concern single case reports, or at most they include several cases, yet the authors draw firm conclusions from such skimpy evidence. Most of these writers, and this includes authors of imposing text-books, accept without question the statement that pregnancy accelerates the growth of a tumor, or that it predisposes to the development of metastases when the tumor has been previously treated. Various factors are blamed, such as the increased blood supply to the cervix, the changed hormone content of the blood, and the dilated lymphatics. Way (1) states that there is little support for these arguments and agrees with Emge (2) that "the growth rate of a neoplasm is inherent in the neoplasm, and experimental evidence substantiates clinical findings that pregnancy does not influence growth rate or size beyond certain reactions, of which retardation is the commonest, but many tumors are unaffected, and a very few may be accelerated."

Emge (2) believed that youth may possess a protective mechanism against tumor growth, and that pregnancy may favor this protective mechanism. This possibility may be deduced from the fact that the number of women with cancer during pregnancy is significantly less than expected. Cancer of the cervix during pregnancy falls far short of the expected number, and for such cancer during pregnancy in women between the ages of 30 and 40, the curability is above the expected average.

Pregnancy must be balanced against age, time, and the location and tissue type of the tumor. There is no proof that pregnancy accounts for either inception of the growth or malignant degeneration.

Emge (2) concludes that the behavior of neoplastic tissue during pregnancy depends upon a complex set of factors, the most important being the inherent growth potential of the tumor which is controlled by a protective mechanism.

* Parts I–XIX of this study were published in the July, August, November (1956), April, May, June, August, October, November (1957), May, July (1958), May, August, September (1959), May, July (1960), and January, February and September (1961) issues of this Journal.

† Attending Physician.

If the balance is disturbed, acceleration or retardation results. The inherent growth potential is impossible to estimate in clinical cases. There is no doubt that neoplastic tissue shares in the general systemic response to pregnancy. If the tumor participates in the local increase in blood supply, its size increases proportionately, but this cannot be considered as true growth. Fibromyoma and certain ovarian cysts show this temporary response based on the ability of the neoplasm to take part in local changes. Certain neoplastic tissues undergo hyperplasia and hypertrophy due to hormonal changes, *e.g.*, adenoma of the breast or leiomyomas of the uterus. This is a true, but limited, growth response.

In summary, Emge (2) believes that, when compared to the incidence in matching samples of nonpregnant women in the general population, the incidence of malignant disease in pregnant women is lower than expected, owing partly to the inhibiting influence of some gestational factor upon initiation of the malignant process.

EXPERIMENTAL STUDIES

Experimental studies in general support the clinical evidence, and in most instances attribute to pregnancy a retarding or impassive role. A variety of tumors was used in these studies, and the findings show that pregnancy affected these tumors in different degrees.

Emge (2) concluded that the growth rate of benign and malignant tumors, although responsive to the general systemic influences of pregnancy as expressed by cytologic changes, is not influenced beyond variation in individual growth propensities.

Morau (3), Loeb (4) and Herzog (5) found that pregnancy stimulated the growth of implanted cancer in experimental animals. Conversely, Loeb found that pregnancy inhibited the growth of a mammary adenoma in the dog. Emge and Wulff (6) found no effect of pregnancy on the growth of a fibro-adenoma and adenoma in the rat. Ehrlich (7), Uhlenhuth and Weidanz (8), Albrecht and Hecht (9), Von Graff (10), Slye (11), Kross (12), Kamekura (13) and Mischtschenko (14), among others, found that pregnancy had an inhibitory effect on a transplanted tumor.

A retardation of tumor growth in pregnancy has been observed in both clinical and experimental series. Several investigators have attributed an inhibitory factor to the placenta and embryonal tissue [Fellner (15), Gross and Wadja (16), Fischera (17)], or to a marked increase in prolan excretion [Zondek and Hartoch (18)].

Ehrlich (7) and Slye (11) believed that "athreptic immunity" was an important factor. This theory based the beneficial effect of pregnancy on withdrawal of nutritional elements from the tumor by the growing embryo. Emge (2) pointed out that this cannot be the only factor, and it can be nullified by the growth rate of the carcinoma mass.

Emge and Wulff (6) concluded from an experimental study that a transplantable mammary adenofibroma of the white rat could respond functionally to pregnancy by undergoing cytologic changes in every way similar to that of

the parent tissue in pregnancy. However, the average time of appearance of the growth, as well as the average daily growth of the tumor material implanted at the period of earliest sex maturity was apparently slightly retarded by pregnancy.

Marchant (19) studied the influence of pregnancy and lactation on the incidence of mammary carcinoma induced with methylcholanthrene in female mice of a strain particularly sensitive to this carcinogen.

Many strains of mice carry a high natural incidence of mammary cancer, partly owing to the presence of a factor transmitted from one generation to the next in mother's milk. In some of these strains, the incidence of mammary tumor has been higher among breeding females than among virgins, indicating that hormonal stimulation also has an influence on tumor development. Other strains of mice, free from the milk factor, carry a low incidence of spontaneous mammary cancer, but it is generally possible to induce mammary tumors in these strains with the aid of carcinogenic hydrocarbons. In the Bonser I.F. strain of mice there is a low natural incidence of mammary cancer, but this strain is very sensitive to carcinogenic hydrocarbons.

TABLE 1

Effect of Pregnancy on Tumor Growth in Various Experimental Animals with Different Tumors

YEAR	OBSERVER	TYPE OF TUMOR	ANIMAL	EFFECT OF PREGNANCY ON GROWTH		
				STIM.	INHIB.	NONE
1894	Morau	Carcinoma	Mouse	+		
1902	Loeb	Mammary adenoma	Rat	+		
1902	Loeb	Sarcoma	Rat	+		
1902	Loeb	Mammary adenoma	Dog		+	
1902	Herzog	Loeb sarcoma	Rat	+		
1904	Bashford and Murray	Jensen sarcoma	Rat			+
1907	Haaland	Various sarcomas	Mouse		+	
1908	Ehrlich	Carcinoma	Mouse		+	
1909	Uhlenhuth and Weidanz	Carcinoma	Mouse		+	
1909	Albrecht and Hecht	Carcinoma	Mouse			+
1914	Von Graff	Sarcoma	Rat			+
1916	Loeb and Fleisher	Mammary carcinoma	Mouse		+	
1920	Slye	Spont. carcinoma	Mouse		+	
1921	O. Frankl	Carcinoma	Mouse		+	
1921	Kross	Flexner carcinoma	Rat		⊕	+
1924	Kok	Ehrlich carcinoma	Mouse		+	
1924	Krotkina	Tar papilloma	Rabbit	+		
1925	Kamekura	Carcinoma	Mouse		+	
1929	Marsh	Spont. carcinoma	Mouse		+	
1931	Mischtschenko	Sarcoma	Rat		+	
1931	Mischtschenko	Carcinoma	Rat		+	
1932	Grauer and Robinson	Fibroadenoma	Rat	+		
1933	Emge and Wulff	Fibroadenoma	Rat			+
1933	Emge and Wulff	Fibroma	Rat			+
1934	Emge and Wulff	Fibrosarcoma	Rat			+

(Courtesy of Emge, L. A.: The influence of pregnancy on tumor growth, *Tr. Am. Gynec. Soc.* **59:** 258, 1934.)

In studying the influence of breeding on the incidence of tumors induced with carcinogenic hydrocarbons, Marchant found that a high incidence of mammary tumors (75 per cent) could be induced in virgin mice of the I.F. strain. No tumors were induced in the naturally breeding mice allowed to lactate before methylcholanthrene treatment began, but the incidence was 29 per cent when treatment began before breeding. These results indicate that pregnancy and lactation have a significant effect in lowering the incidence of induced mammary tumors in I.F. mice. The protective effect of lactation in this strain makes it worthy of further study.

Some effects of pregnancy on tumor growth are listed in Table 1. It may be seen that different tumors exhibit different degrees of susceptibility to the influence of pregnancy. These results represent differences in individual tumor behavior. Especially noteworthy are the effects noted by Loeb with transplantable adenofibroma in the white rat and in the dog.

CANCER OF THE BREAST ASSOCIATED WITH PREGNANCY

Carcinoma of the breast in pregnant women has generally been considered a hopeless disease. Haagensen and Stout (20) were unable to find a single five-year survivor without residual disease; in fact, they included carcinoma of the breast during pregnancy and lactation in their "criteria of inoperability." More recently, Haagensen (21) concluded that radical mastectomy may be justified in these patients if the disease is locally operable.

Rosenthal (22) reported 3 cases of carcinoma of the breast associated with pregnancy, and considered them to confirm the belief that pregnancy stimulates the growth of cancer of the breast and hastens the fatal outcome. He thought that it would be a safe view to regard pregnancy and lactation as probable aggravating factors in all cases of cancer of the breast, and this would call for the earliest possible diagnosis and treatment.

Cheek (23) sent a questionnaire concerning carcinoma of the breast during pregnancy to 55 physicians considered to be well informed on this subject. The survey indicated that although the results of treatment of carcinoma of the breast in pregnancy were disappointing and the prognosis was poor, it was not invariably hopeless. None of the respondents considered pregnancy itself as an absolute contraindication to surgery. Some of the physicians thought that termination of the pregnancy was indicated, particularly if the cancer was discovered during the first half of gestation. There was general agreement that subsequent pregnancies should be avoided by women who had received treatment for mammary cancer. Whether pregnancy could increase the chances of carcinoma developing in the remaining breast remained an unsettled point. There was unanimous opinion that obstetricians should examine the breasts of their patients at frequent intervals.

Geschickter's (24) experience coincided with that of some other investigators. Of 15 women with breast cancers and pregnancy, all had axillary metastases, and in 13 death followed within three years. Thirty-seven patients with breast cancer were operated on during or shortly after lactation; the five-year survival

rate was 21 per cent, which indicated a considerably better prognosis than when breast cancer occurred during pregnancy.

Lewison (25), in a collective review, concluded that the co-existence of breast cancer and pregnancy is fraught with grave peril. Although the situation is indeed grim, the prognosis is probably as good as that for nonpregnant patients of similar age who have the disease to a similar extent.

In a comprehensive review of 4,628 cases of breast cancer treated at the Mayo Clinic, Harrington (26) noted 92 women who were either pregnant or lactating at the time that the cancer was discovered. The average age for this group of women was 36.6 years and an unusually high percentage (84.8 per cent) had axillary metastases, whereas in the entire series of Mayo Clinic breast cancer patients (pregnant and nonpregnant) only 63.8 per cent had axillary metastases at the time of operation. The five-year survival rate for patients with axillary metastases was only 5.7 per cent, and the ten-year survival rate was only 3.4 per cent. In contrast to this gloomy picture, the five-year survival rate for the patients who had *no* axillary metastases was 61.5 per cent, and the ten-year survival rate was 40 per cent. This compares favorably with the rate for nonpregnant breast cancer patients without metastases in the same age group. Obviously, the aim should be to diagnose and treat these patients before metastases have occurred.

Harrington's survey also showed that of 55 women who became pregnant subsequent to operation for breast cancer, 30 were traced who did not have axillary metastases; of these, 29 survived more than five years; and of 25 additional patients traced, 22 survived for more than ten years. This extremely good showing, however, is an artifact because women with the most serious types of malignant tumors probably do not survive long enough to become pregnant. Indeed, the incidence of axillary metastases in this group was only 45 per cent, compared to 63.8 per cent in the entire Mayo Clinic series of breast cancer patients.

White (27) studied the world literature on carcinoma of the breast in the pregnant and nursing patient, and found 1,375 cases. Carcinoma of the breast complicated pregnancy about 3 times per 10,000 pregnancies. Pregnancy complicated breast carcinoma about 3 times per 100 breast carcinomas.

The gross five-year survival rate (59 per cent) and the ten-year survival rate (41 per cent) for 268 patients treated for carcinoma of the breast prior to pregnancy was comparable to or better than the gross survival rate for nonpregnant patients.

Of 804 patients treated for carcinoma of the breast coincidentally with pregnancy or nursing, 13.4 per cent survived five years and 8.6 per cent survived ten years. For patients treated for carcinoma of the breast coincidentally with pregnancy since 1941, the ten-year survival rate was 21.5 per cent in the absence of metastases. Patients with metastases treated during pregnancy or during nursing had 5 to 20 times as poor a prognosis as those without metastases.

Abortion (in 108 patients) did not have a clear effect on the course of carcinoma of the breast complicated by pregnancy.

Austin (28) reported 9 cases of breast cancer associated with pregnancy, noted in his own practice in the prior ten years; in 8 there was axillary spread.

Of these 8 patients, none survived five years, whereas the sole patient without axillary spread was alive and well eight and a half years after operation. Austin believed that certain known factors predispose to the poor prognosis in pregnant patients with breast cancer. One of these is the patient's delay of two or more months in seeking medical aid, and a further doctor's delay of one month before treatment. The tumor may be masked by the increased size of the breast. The increased vascularity of the breast probably increases the spread. The youth of the patient is an important factor; cancer in the young is always very serious. The average age of the pregnant breast cancer patient is 36.6 years. The hormonal effects of pregnancy on breast tissue are pronounced, and some of these hormones may affect the breast cancer.

Authorities differ in opinion on the subject of whether a person treated for breast cancer should ever again become pregnant. Most believe that subsequent pregnancy has a deleterious effect. Harrington (26) and White (27), reviewing the literature and studying their own cases, concluded that subsequent pregnancy has no effect on the final outcome of the breast cancer.

Brown (29) stated that in 1949 he saw a woman previously treated for carcinoma of the breast, who was two months pregnant. In this woman, and in 2 other similar cases, abortion was performed. All of these women died within a relatively short time. During the intervening years, Brown accumulated 20 cases, which he reviewed. Eleven of the women are still well. The longest survival so far has been fifteen years. Neither interrupting the pregnancy nor allowing it to go to term has affected the outcome in any of the patients.

Smith (30) is one of the few authors who thinks that interruption of pregnancy in a patient with breast cancer is actually harmful. He noted a slower tempo of tumor growth during pregnancy, with an acceleration following delivery or abortion. Hochman and Schreiber (31) believe that pregnancy does not enhance the malignancy of an existing tumor. These authors studied 40 pregnant patients with breast cancer and found a 40 per cent five-year survival rate. This rate corresponds well with that for nonpregnant patients with breast cancer.

Finn (32) believed that one reason for the *apparent* rapidity of growth of breast cancer during pregnancy is that usually the cancer antedates the pregnancy and is already in an advanced stage at the onset of pregnancy. The pregnant woman is more likely to have an infiltrating or solid type of cancer, and both of these types are more malignant histologically and metastasize more rapidly.

In summary, cancer of the breast as usually found in the pregnant woman is further advanced when first seen than in the nonpregnant patient. However, for pregnant patients with breast cancer and no metastases, the survival rate compares favorably with that for nonpregnant patients of similar age with the same degree of disease.

CANCER OF THE CERVIX ASSOCIATED WITH PREGNANCY

According to reports from all over the world, cancer of the cervix is the most common malignant growth found in the pregnant woman. Emge (2) stated that

it is about seven times more common than breast or rectal cancer, and about ten times more common than osteogenic sarcoma, which is a disease of the young. Emge wondered why cancer of the cervix should be so much more common than other cancers during pregnancy, especially since it occurs more often in the nonpregnant woman past the age of 35. He did not believe that trauma, though the most obvious explanation, is necessarily the true one.

Some observers reported that lesions diagnosed as pre-invasive cancer of the cervix during pregnancy disappeared spontaneously at the termination of pregnancy, the inference being that these were "pregnancy changes" and not true pre-invasive carcinoma. Greene and his associates (33), however, take the stand that pregnancy does not cause specific change in the cervical epithelium. They grant that metaplasia and hyperplasia of the glandular elements is more common and more prominent during pregnancy than in the nongravid state; that the surface stratified squamous epithelium of the cervix grows rapidly during pregnancy; and that a mild increase in the thickness of the basal cell layer with normal nuclei is occasionally seen. When the criteria are present for the diagnosis of pre-invasive carcinoma, the diagnosis should be made whether the patient is pregnant or not. The controversy about pre-invasive carcinoma in pregnant patients can be solved only by deliberately following patients with such lesions and determining whether these lesions disappear after delivery. In 14 pregnant patients, Greene *et al.* diagnosed pre-invasive carcinoma of the cervix from biopsies. The lesion persisted after the termination of pregnancy in 12 patients and was found in either biopsy or operative specimens. Thus, with 2 exceptions, these lesions (whether they were true carcinoma or not) were not pregnancy changes and did not disappear after the termination of pregnancy. In 2 of the 14 patients, these authors were not able to find any abnormality post partum, and considered the possibility that the lesions were not true pre-invasive carcinoma but were reversible changes.

One hundred and thirty-six cases of cervical carcinoma associated with pregnancy were analyzed by Kistner, Gorbach and Smith (34). About 1 per cent of all cervical cancers occurred in pregnant women or within four months after delivery. Pregnancy was complicated by the disease about once in every 2,000 cases. The average age of the patients was about 33 years, and the average parity about 5. The authors stated that most of the cancers were squamous in type and moderately well differentiated. Carcinoma in situ should not be definitely treated until studies are made following delivery.

In the series of Kistner *et al.*, when stage I and stage II cancers were treated during the first two trimesters, the results were excellent. Accordingly they inferred that cervical cancer is not aggravated by pregnancy before the middle of the third trimester. In clear contrast, were the poor results among those treated at term or within four months after delivery. From their data, it seems valid to conclude that certain changes in relation to the termination of pregnancy make cervical cancers lethal.

From 1931 to 1959, there were 81,806 obstetric patients at the Chicago Lying-in Hospital, and Hayden (35) found only 12 cases of cervical cancer among them

(.014 per cent). Carcinomas in the more advanced stages directly paralleled the later stages of pregnancy. The absolute five-year survival rate for these patients was 50 per cent, and the ten-year rate was 25 per cent. These survival rates are similar to those for women in the nonpregnant state.

Hayden stated that although there is no doubt that carcinoma in situ exists as a clinical entity, its exact status is still undetermined, especially in the presence of cervical changes associated with pregnancy.

Johnson and her co-workers (36) reported their findings on pre-invasive cervical lesions in obstetric patients. The effects of time, removal of cervical tissue by biopsy, and pregnancy per se, were studied in a series of 119 cases of anaplasia. Tumors that regressed, did so within eighteen months of the discovery of the lesion. Only one lesion progressed to carcinoma in situ. Anaplasia recurred in 6 cases which had apparently regressed. Although 4 lesions that were discovered during pregnancy apparently progressed to early stromal invasion, this was thought to be coincidental.

Galvin, Jones and TeLinde (37), in an article on the clinical relationship of carcinoma in situ and invasive carcinoma of the cervix, drew the following conclusions:

1. Carcinoma in situ is potentially invasive and, if untreated, may progress to clinically evident cervical cancer.
2. Clinical cervical cancer is preceded by carcinoma in situ in too large a proportion of cases to be coincidental.
3. The clinical course of cervical cancer represents a small segment of its life history; the greatest part of its existence is in the pre-invasive stage.
4. If a cervical biopsy specimen is obtained within five years before the development of clinical cervical cancer, it will likely show carcinoma in situ.

Jones (38) discussed the communication of Dr. John E. Dunn on the natural history of uterine cancer. On the basis of data obtained during the screening of 53,585 women, Dunn had investigated the following points:

1. The relative incidence of carcinoma of the cervix among Negro and white women.
2. The duration of asymptomatic invasive cancer to the time of normal diagnosis.
3. The duration of carcinoma in situ.
4. The discovery of invasive cancer in some patients one year after negative results with cytologic tests.

The data indicated that, for unknown reasons, symptomatic cancer was 1.6 times as prevalent among Negro as among white women. Three or four years elapsed from the beginning of stromal invasion to the time of usual diagnosis. A period of 4.5 to 5.0 years seemed to be the duration of cancer in situ before development of invasive cancer. This fits well with an estimation made from the average age of patients with carcinoma in situ as compared with the average age of patients with invasive cancer. The average age at which carcinoma in situ appears is about 38 years, and the average age at which invasive carcinoma appears is about 48 years. The discrepancy can be rationalized as follows:

Carcinoma in situ lasts about five years, and it takes three to four more years before a clinical diagnosis is made. Dunn found that in about one-quarter of the invasive cancer patients the results of cytologic examination had been normal one year previously. This group may not have had in situ precursors or, alternatively, the previous year's cytologic findings were falsely negative.

In summary, it appears that pregnancy initiates cellular changes in the cervix which are very similar to those found in carcinoma in situ. However, these changes are completely reversible in the great majority of pregnant women. Emge (2) stated that even when a diagnosis of carcinoma in situ has been established in a pregnant woman, the patient should be managed conservatively, because postpartum examination may fail to show any evidence of cancer. The nature of carcinoma in situ is still obscure, and there is good evidence that some lesions are reversible, especially during pregnancy. Is this reversibility more common in pregnancy, and if so does pregnancy supply some factor necessary for the reversion?

MALIGNANT MELANOMA OCCURRING DURING PREGNANCY

Pack and Scharnagel (39), in reviewing 1,050 cases of malignant melanoma, found 36 in pregnant women. Sixteen of these 36 women died of melanomas within three years, although they had adequate treatment. Eighteen women were alive two years after treatment. Two others were alive and well without evidence of disease, eight and thirteen years after therapy.

George, Fortner and Pack (40) reported on 413 female patients with melanoma seen at the Memorial Center. Of these women, 77 were pregnant coincident with melanoma, and 38 were pregnant after melanoma; 141 patients aged 16 to 43 years acted as a control group, and 189 patients age 44 to 88 acted as an older control group.

The study revealed a peak incidence of melanoma in the 31 to 35 year age group. The lower extremities were the most common site of lesions in all groups.

Survival rates in pregnant and nonpregnant patients were approximately the same, with five-year and ten-year rates of 47 per cent and 42 per cent respectively for the whole group. The data did not permit statistical analysis to determine if the association of melanoma and pregnancy was any more frequent than would be expected.

These authors cited several cases of regression of extensive melanoma associated with pregnancy. In 2 of these cases there was placental involvement with melanoma, but the children were spared. If early adequate treatment is given, the prognosis is the same as in the nonpregnant woman.

Allen (41) reported on an intriguing situation sometimes observed in malignant melanoma. In such a case, metastases developed as a direct response to the stimulus of pregnancy, and seemed to be so dependent upon the stimulus, that upon its withdrawal the metastases disappeared. The speed of the disappearance was remarkable, in that regression became clinically complete within eleven weeks after delivery. The patient was a white woman, aged 43, in whom recurrent tumors had been treated by surgical excision followed by radiotherapy.

When she was seen again she was seven months pregnant, and had numerous recurrent nodules. These were also excised. Fourteen days after delivery, more nodules appeared, but these were not removed. Eleven weeks after delivery, recovery was complete.

In a letter to the Editor of the British Medical Journal with regard to Allen's article on the effect of pregnancy on the growth of melanoma, Pegum (42) makes an interesting comment. Allen's patient had rather widespread recurrent malignant melanoma nodules which increased in size and number during pregnancy, but regressed following delivery. Pegum believed that the most probable explanation of the increased growth during pregnancy was the temporary increase in secretion of melanocyte-stimulating hormone (MSH) in pregnancy. If so, then Pegum pointed out two available means of depriving these tumors of MSH: 1) removing or destroying the pituitary gland and maintaining health by giving substitute hormones; and 2) administering cortisone, which probably inhibits MSH secretion, as shown by the disappearance of pigmentation in Addison's patients during cortisone therapy.

Since Shizume and Lerner (43) showed that the blood and urine levels of MSH were elevated during pregnancy, Varon (44) attempted to isolate MSH from the human placenta. Although the activity of this hormone was less than the activity reported for pure MSH from hog pituitary, it was still considerable. Such hormonal activity may account for the spread of melanoma during pregnancy.

Berlin and Winters (45) described a case of malignant melanoma of the vulva with pregnancy; the patient had survived six years at the time of the report. They considered this to be an apparent cure, maintained during three successive pregnancies. This patient, aged 28, had a dark lesion on the right labium which was thought to be a hemangioma; it was desiccated with carbon dioxide snow. The patient became pregnant but had a spontaneous abortion. The lesion recurred and was excised. The diagnosis was melanoma with malignant tendencies. One year later, another lesion excised in this area was diagnosed as malignant melanoma. A radical vulvectomy was performed, with dissection of the right groin and resection of the nodes from the femoral canal to the bifurcation of the aorta; these nodes contained no metastatic tumor. Three years later a second primary malignant melanoma was removed from the patient's back. Six years after the first operation, she became pregnant and had no recurrence. The next year she became pregnant again. No further melanomas were found.

Parkes-Weber, Schwartz and Hellenschmied (46), as well as Holland (47), reported a patient who was delivered while dying of multiple metastases from malignant melanoma of the thigh. The placenta showed numerous metastases. The child died when less than 1 year old, and its liver and several lymph nodes contained deposits of melanoma identical in structure with the mother's tumor. This seems to be the only recorded case in which the tumor was found in mother, placenta and child. The placenta is invaded only on extremely rare occasions with other types of tumor metastases.

Mulla (48) observed a case of malignant melanoma during pregnancy. The

patient was a 37-year-old woman who had had two moles excised; they were diagnosed as benign nevi. She went through one pregnancy without any extraneous difficulty. During the fourth month of a second pregnancy, she noted two nodules, one on the scalp and one at the previous site of a nevus. The nodules enlarged during pregnancy. These tumors and several nodes were excised, and proved to be malignant melanoma. Mulla remarked that in other cases the patients also had noted the appearance of malignancy in the fourth gestational month, at the time when the pituitary is stimulated by the placenta.

White (49) started an investigation regarding the possible differences in the growth of melanoma between men and women, when it was learned that melanomas, after transplantation in two strains of mice, grew 4 or 5 times as large in males as in females during the same period. Survival in cases of human melanoma was studied in 439 instances. The distribution was roughly equal for the two sexes, but survival was longer in women than in men and this difference was statistically significant. Women with melanoma have a greater chance of living for five years, and the prognosis for survival beyond the five-year period strikingingly favored the women. Thus it is probable that melanoma is under some forms of hormonal control.

In summary, almost all authorities believe that pregnancy acts as a growth stimulus for melanoma. However, in patients who survive pregnancy, there has been more than an occasional instance of regression. These regressions do not appear to be coincidental—a most challenging concept.

MISCELLANEOUS MALIGNANT STATES ASSOCIATED WITH PREGNANCY

Levine and Weiner (50) reported an unusual case of a 34-year-old primipara who was delivered after a short labor. However, weakness, colicky pains in the abdomen, vomiting, and loss of weight developed soon after her discharge from the hospital. Three months later, a large tender, fixed mass was found in the mid-abdomen. Laparotomy was performed four months post partum, and free hemorrhagic fluid, a liver with metastatic nodules, and multiple implants on the peritoneum and omentum were found. There was also a large firm mass involving the transverse colon and the gastrocolic omentum. The pathologic diagnosis (several biopsies) was metastatic adenocarcinoma. After a stormy course, the patient improved and was discharged. When seen again two weeks later, the abdomen was distended with free fluid, the liver was enlarged, and other masses were felt in the abdomen. She remained under observation and continuously showed improvement.

Three years postoperatively she was found to be pregnant. In view of the previous history, it was decided to terminate the pregnancy by abdominal hysterotomy and sterilization. At operation, the liver was normal and there were no implants in the peritoneum. Some small subperitoneal elevations were seen on the fundus of the uterus, so a total hysterectomy was performed. Microscopic sections from the uterus, tubes, ovaries, and omentum revealed no evidence of cancer. There had been no recurrence up to the date of writing, four and a half years after the first operation. This extremely interesting case of

regression unfortunately cannot be analyzed further, because of the paucity of clues.

Frenkel and Meyers (51) reported on 8 pregnant women (16 to 29 years of age) with acute leukemia, whom they had seen in the previous five years. Two maternal deaths occurred before term. One patient died during delivery and 4 patients died from one to nine months after delivery. One patient is still alive and in a state of complete remission, five years after the diagnosis of leukemia. Five living, healthy infants resulted from these pregnancies. The observations of these authors support the concept that pregnancy per se exerts no specific effect on the course of acute leukemia, except insofar as early pregnancy imposes an obstacle to vigorous therapy. The adjuvant use of steroids is recommended in patients in whom bleeding or toxicity is a significant feature.

DISCUSSION

Emge (52) believed that pregnancy does not invariably hasten or stimulate tumor growth. Carcinoma of the uterus associated with pregnancy is extremely infrequent and usually involves the cervix. Emge found 6 cases in 11,600 pregnancies, or an incidence of 0.05 per cent, which agrees with the rates generally found in the literature. Peller (53) compared the expected number of cancers in pregnant women with the actual incidence, and found the latter significantly lower than expected. Peller concluded that pregnancy leaves the general body structure more resistant to the development of cancer, raises the average age for onset of cancer, and retards its progress, and that this is the expression of a protective mechanism, either produced or intensified by gestation.

Peller substantiated the opinion of Mayer (54), who believed that pregnancy does not favor the growth of cervical cancer, but rather restrains its spread, and increases its operability and curability.

Ehrlich (7) contended that the activity of the neoplastic cell is inhibited by the greater activity of the fetal cell mass. If, in spite of this inhibition, the cancer mass manifests violent growth, the protective mechanism must have been insufficient.

Others believe that pregnancy does not necessarily increase the degree of malignancy or favor the spread of cancer. In fact, dependent upon the type of cancer, the age of the host and the period of discovery, pregnancy may be considered a favorable factor. Still others conclude that although pregnancy may not hasten the growth of cervical cancer, yet it may favor its spread because of the favorable conditions created by the increased blood and lymph supply.

Cancer in young pregnant women oftimes assumes a very rapid course. However, this is not because of the pregnant state, but because the cancer occurs in a young individual. If pregnancy were an exciting factor in uncontrolled tissue growth, it would be reasonable to expect cancer to occur in some patients with ectopic gestation, but this is an extremely rare occurrence.

Emge (2) believed that although the local increase in the blood and lymph supply incident to pregnancy offers a more fertile soil for invasion by neoplastic growth, it also favors operability and therefore curability. Emge personally

treated 6 cases of carcinoma of the cervix associated with pregnancy and obtained a high percentage of cures.

Emge found only 1 case of mammary cancer in 11,600 pregnancies. The patient was a 46-year-old gravida VIII, who underwent radical mastectomy and was treated with massive x-ray therapy. She became pregnant two months later, and about one month after this a local recurrence developed. Then the cancer became generalized and progressed rapidly. The patient died twelve days after a premature delivery. Emge believed that gestation probably enhanced the virulence of this growth.

Ovarian tumors were found to be co-existent with pregnancy in about 0.4 per cent of Emge's series. Cystomas were the most frequent, dermoids the next most frequent, and malignant tumors extremely rare.

Peller and Stohr (55) stated that cancer of the gastro-intestinal tract grows more rapidly during pregnancy. This tumor rarely occurs during gestation. When gastro-intestinal cancer occurs in the young, it is extremely virulent. Apparently the age of the patient is the important factor.

Brain tumors are rarely found during pregnancy. There have been cases in which the symptoms appeared with pregnancy, then totally disappeared, only to recur during subsequent pregnancies. The recurrence may be a manifestation of the ability of nerve tissue to take part in the general cellular response to pregnancy.

Way (1) pointed out that when comparisons are made of the survivals of pregnant and nonpregnant women with carcinoma of the cervix, the only suitable controls are nonpregnant patients under the age of 40, because it is in this age group that pregnancy complicates these tumors. When studied in this manner, Way found that the survival rate for the pregnant patients treated more than five years previously was 33 per cent, whereas for the nonpregnant patients below the age of 40, it was only 19 per cent.

Sadugor, Palmer and Rheinhard (56) showed that in 124 patients with carcinoma of the cervix complicated by pregnancy, the results of treatment were the same as in nonpregnant patients with the same degree of the disease and in the same age group.

At first carcinoma of the cervix grows slowly, and later the curve of development is very rapid. Way states that when a tumor progresses at a rapid rate during pregnancy, the cause lies in the coincident rapid rise in the tumor growth rate curve, and not in the pregnancy. There is no reliable evidence that pregnancy per se can cause an alteration in the growth rate of the tumor.

Carcinoma of the breast is less common in association with pregnancy than is cancer of the cervix. The prognosis for breast cancer is worse in the younger age groups, because younger women have more anaplastic and more advanced tumors. Schreiner and Wehr (57) noted that of 14 patients with breast cancer who were under 30 years of age, only 3 survived more than one year.

Smith (58) analyzed his cases of cancer associated with pregnancy and found 22 patients with breast cancer who had survived from one to fifteen years; in the 7 who had died soon after treatment, the cancer had been far advanced when the patients were first seen.

In Way's (1) series, all of the cases were far advanced when first seen, so understandably the results were poor. One patient who refused treatment and had two successful pregnancies died eighteen months after the second pregnancy.

Thus the survival rate for either breast cancer or cervical cancer in the pregnant woman compares favorably with the rate for these cancers in the nonpregnant woman, provided the comparison is made between patients in the same age group and in the same stage of the disease.

SUMMARY

When compared to the incidence in matched samples of nonpregnant women in the general population, the incidence of malignant disease in pregnant women is lower than expected. This may be due to the influence of some gestational factor upon initiation of the malignant process.

Cancer of the breast in pregnant women is usually farther advanced when first seen than in nonpregnant women. However, when lesions in the same stage are considered, the survival rates compare favorably.

Pregnancy initiates cellular changes in the cervix which are very similar to those found in carcinoma in situ. These changes are completely reversible in the great majority of pregnant women.

Pregnancy acts as a growth stimulus for melanoma. Regression sometimes occurs after the termination of pregnancy.

Physical changes observed in benign tumors during gestation are not necessarily expressions of growth.

Pregnancy does not favor the inception of malignancy or cause malignant degeneration of benign tumors.

Pregnancy usually does not influence the growth rate or the size of a neoplasm, but if it does, retardation is the most frequent result. In many instances the tumor remains unaffected and only occasionally is acceleration observed.

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MOTIVATION AS A HEALTH RESOURCE*

JACK WEINBERG, M.D., F.A.P.A.†

University of Illinois School of Medicine and Michael Reese Hospital, Chicago, Illinois

"We both agree that the mind is the measure of the individual; the quality of life as it reaches its zenith in time may be determined by mental content and meaningful activity," Dr. Bortz (1) wrote to me when he invited me to discuss motivation as a health resource, before our Society. Thus did Dr. Bortz succinctly paraphrase another eloquent and eminent American physician, Dr. Benjamin Rush (2), who in 1789 in an extremely interesting essay "On Old Age" had the following to say: "It has long been an established truth, that literary men (other circumstances being equal) are longer-lived than other people. But it is not necessary that the understanding should be employed upon philosophical subjects to produce this influence upon human life. Business, politics, and religion which are the objects of attention of men of all classes, impart a vigor to the understanding, which, by being conveyed to every part of the body, tends to produce health and long life." The wisdom of the foregoing remarks and their applicability to modern psychosomatic concepts is unassailable. What remains is the never-ending effort to put into practice these theoretical considerations.

Both Dr. Bortz and Dr. Rush imply that of all living creatures man alone has the God-given gift of mentation and imaginative capacities. These give man the unique opportunity to influence his environment, help shape his own future, affect the course of his life, and effect the inevitable. Thus, man of all living matter, actually has the freedom to act and to "choose" between success and failure, health and disease.

Real freedom of action or freedom of choice, however, is given only to a few. For choice, as the psychiatrist sees it, is dependent not only upon the conscious evaluation of any given situation but more cogently upon the unconscious motivation underlying the apparent thought processes. Indeed the voice of the intellect is soft when pitted against the tumultuous clamor of the individual's unconscious emotional stresses and drives. It is only when one is aware of one's unconscious motivations and one acts in concert with them or takes a firm stand against them, that one can be said to have a free choice. Successful living is therefore a product of the utilization of the proper emotional motivation.

In later life the will to live and adapt to stressful life situations (which is the real measure of health) is often undermined by unconscious drives which are

* Presented at the 18th Annual Meeting of the American Geriatrics Society, New York, N. Y., June 22–24, 1961.

† Associate Professor of Psychiatry, University of Illinois School of Medicine; Attending Psychiatrist, Psychosomatic and Psychiatric Institute for Research and Training, Michael Reese Hospital.

Address: 30 North Michigan Avenue, Chicago, Illinois.

inimical to the interest of the organism. Whatever the etiologic factors (and these may be as varied as are human beings), many aging people present a little-recognized phenomenon which I like to call *the preparation for death.* This is characterized by a gradual withdrawal on the part of the organism from participation in the ongoing life processes. There is a withdrawal of feelings for, and investment in meaningful objects, animate or otherwise; a loss of interest in life and the environment; a mounting preoccupation with inner painful stimuli; and an overwhelming wish for the termination of life but not by "one's own hand." If not by one's own hand then by *one's own mind.* By this disengagement from life the organism behaves as if it is preparing itself for final isolation and death.

Although we as physicians may view the foregoing as sick behavior and morally untenable within our Judean-Christian culture, these people regard it as morally justifiable within the very same frame of reference. It is their strict conscience—the strict superego in my discipline's jargon—which precludes their continued living in a society to which they feel they contribute nothing and from which they can expect nothing. In a society which still condones capital punishment, they sentence themselves to the extreme punishment for guilts, real or imagined. However, this is not the sole determinant for their egregious behavior. They are lessening the fear of the non-existence which death implies, by gradually leaving life, negating its pleasures, and making death more acceptable by accenting the "slings and arrows of outrageous fortune." Thus, true to the concept of the polarity inherent in all behavior, the withdrawal from life is also a preparation of the self and others to the idea of one's death and non-being.

Death, as the physician knows, may hold no terror for many, and may even be welcomed and considered as a friend. Indeed, in a moving letter to his father before the latter's death, Mozart (3) wrote lyrically of death and beautifully illustrated my point: "Since death (properly understood) is the true ultimate purpose of our life, I have for several years past made myself acquainted with this truest and best friend of mankind so that he has for me, not only nothing terrifying anymore, but much that is tranquilizing and consoling.

"And I thank my God that He has bestowed on me the good fortune to provide the opportunity (you understand me) of recognizing death as the key to our true blessedness.

"I never lie down in my bed without reflecting that perhaps I (young as I am) shall never see another day; yet none of all who know me can say that I am socially melancholy or morose. For this blessing I daily thank my Creator and wish it from my heart for all my fellow men."

It could be pointed out that Mozart of all people could afford to write with composure of death, for he himself was and is immortal. However, he does quite forcefully affirm Simmel's (4) contention that death is to be reckoned with, not only in the last hour of life, but as rather a formal quality of life itself, coloring all of its contents. Certainly it is safe to state that since man as soon as he comes into being is also immediately old enough to die, he rarely makes any major, if not minor, decision without both his life and eventual death playing a

role in it, consciously or otherwise. All of his plans, activities, precautions and insurance devices reflect this truth. What is germane to my discussion is the added fact that in later life all of these factors become increasingly poignant and take on special meaning. To know the nature of the enemy, to know what one has to overcome gives the individual more courage "to take up arms against a sea of troubles and by opposing end them."

THE CRITERIA OF MENTAL HEALTH

To counter these phenomena are the life-giving, health-sustaining activities which are based upon motivations deeply rooted in the life-thrust inherent in all living matter. These activities, the mainsprings and mainstays of emotional health, must be practiced and continually enhanced throughout one's life. They are a call to arms within the reasonable grasp of every human being concerned with mental health. Furthermore they have been tested and found to be reliable by those who had grown in their years. These, then, are the criteria of mental health:

1. *The best possible physical health*

The physically handicapped or ill person withdraws his psychic energy and his emotional investment from the world in which he lives, and focuses it upon his internal painful stimuli. He listens, so to speak, to that which goes on inside of him and becomes inattentive to the ever-demanding environment. Should he become entranced by the siren call of his aches and pains, pathologic changes commence in the form of disruption of the normal adaptive mechanisms.

Research on the aging process forces upon the investigator the conclusion that a gradual loss of functioning tissue makes a major contribution to impairments in later life. Not all physiologic functions show progressive changes with age; however, significant changes may be demonstrated in many functions even when tested in a resting state. Then too, the aged show greater displacement under stress and a slower rate of recovery, though there are wide individual differences in the effect of age on the reaction to physiologic stress. The investigator of the aged is also compelled to assume that a breakdown in the regulatory mechanism of the human organism, whether neural or endocrine in character, plays an important role in aging.

We have just heard Dr. Shock state: "It is apparent that the older individual is characterized by lower energy output based partly on a loss of functioning tissue and partly on a reduction in the activity of cellular enzymes concerned with energy transformations. In addition, age brings with it a reduced rate of energy mobilization and a reduced efficiency or operation at high or low rates of energy output."

When these changes and defects do occur and make their effects felt upon the entire organism so as to disrupt its functioning, it is imperative to recognize that the disruption is not merely physiologic but also psychologic. We must not only pay lip service to, but act in consonance with, this recognition. As a matter of fact, the emotional disturbances may be so enormous as to overshadow and mask an obvious organic disease.

A number of years ago a 68-year-old woman who had been continually in an institution for a period of twenty years was referred to me by her daughter. The outstanding symptoms were extreme agitation, confusion, destructiveness and paranoid ideation. The latter became especially marked in the last few years of hospitalization, as her vision began to fail. On admission to our hospital and upon thorough physical evaluation (as is my wont in all aged patients), a diagnosis of thyrotoxicosis and bilateral cataracts was made by the consulting staff. Surgery for both conditions was recommended and performed, with the precaution of not operating on both eyes at the same time. The results were spectacular, in that all psychotic symptoms cleared up and what emerged was a woman who had seemed to be asleep for twenty years. To date there has been no recurrence of the psychosis.

A recent report from St. George Hospital in London by Herridge (5) indicates that the foregoing case is not a singular experience. In a study of 209 psychiatric in-patients he stressed the danger of being misled by spurious psychic origins and thus overlooking organic disease. In 5 per cent, a major physical illness first discovered on admission to the psychiatric unit, was the principle diagnosis. In 21 per cent, the physical condition contributed to the onset of the psychiatric illness. Thus, the need for a full physical examination in every psychiatric case irrespective of the source of referral, is of the essence.

These considerations, though elementary and familiar, nevertheless need restatement, for much too often the apparent is neglected because of its very simplicity. Motivation for satisfactory adaptation, let alone for zestful living, can be impaired by deficits over and above the expected physiologic and anatomic changes. These deficits should therefore be remedied to allow the healthful life processes full play and action.

2. *Varied sources of gratification*

Gratification, or the hope for achievement of it, is of vital importance in the stabilization of the psychic economy. It is the hope for a "better tomorrow," for a period of pleasurable experiences and satisfaction, that gives the ego (or the problem-solving self, as I prefer to call it) the motivation and drive for continued integration, effort and energy. The sources of these satisfactions must perforce be varied, for when one source fails or dries up, there must be another to take up the slack, to fill the void, and provide for the necessary needs.

One cannot rely solely on outer supplies for satisfaction. The dependence on other people (family or friends) or objects (such as money), though necessary to supply pleasurable experiences, can easily fail the aging organism. Self-reliance and the development of inner sources of self-respect and gratification become the function of each person during his lifetime. Obviously, too, the goal of medicine and its practitioners is one of the mobilization and exploitation of the individual's resources; the more resources available to the individual (and therefore to the physician), the greater the chance of success. Among the various sources of satisfaction, those which are the most significant for mental health and are at least partly attainable through concerted effort, are the following:

Work—preferably regular. Not considered here is the manifest and compelling

reason for working, the obvious economic one. Equally compelling are the physiologic and symbolic meanings which work has assumed in the imaginative and fertile mind of man. In a previous publication (6), I discussed motivation for retirement and work, and listed some of the meaning that work has assumed. Originally man conceived of work as a punishment—the Biblical story of Adam is ample proof of that—but as is his custom, man transformed this curse into a blessing, for certainly idleness is now the curse and work is the blessing. A job or work constitutes further data by which a man is identified—a frame of reference for further human interaction—thus bestowing on him an identity without which life is intolerable. To reply to the usual question upon introduction, "What do you do?" with an embarrassed, "Nothing" may and often does imply that the person *is* nothing.

Work supplies status and enhances a person's attractiveness to others. Legion are the number of people to whom work has become the medium for social interchange and communication; when removed from it, they are completely lost. A job, whether part-time or full time, enables some people to avoid boredom and introspection, as far too many of us have trouble facing ourselves or bearing our own company. How to "kill time" before it kills them seems to be answered for many by regular employment. Another aspect of the work situation is that it enables the individual to channel his aggressive impulses into sublimated constructive activity. It drains off muscular irritability, a characteristic of living matter, into meaningful patterns of behavior which otherwise may become meaningless and therefore frightening. Above all, work may be a source of intrinsic enjoyment. This is particularly true of those who are in the professions, or of anyone who takes pride in that which he fashions and is able to identify with it.

Creative channels. Although most of us are not gifted in the creative arts, and most of us would go into a panic if a brush were thrust into our hands and we were told to paint on a blank canvass, the fact remains that we are capable of much more than we accomplish. As in athletics, most people will not become professionals, but with practice and perseverance a reasonable adeptness is developed. There is no question but that the same perseverance in the arts can produce highly gratifying results. Some degree of preoccupation with those values which are timeless in scope can lend tranquillity and a proper perspective of the self in the scheme of things. In later life, when physical energies must be conserved, participation in creative activity (preferably active rather than passive, but neither should be avoided) can be highly gratifying and meaningful.

Social responsibilities. Benjamin Rush has already been quoted on the wisdom of maintaining social responsibilities. What needs to be added is that responsible participation in social activities is not only of narcissistic value. It gives the aging person the opportunity for work and achievement in areas that are not bounded by time, and helps him to identify with a timeless continuum and provide tasks which by their very endlessness invite a never-ending challenge. Moreover, it is the continued responsibility of the aging patient to help make the world in which their children live, a decent and safe environment for the

human being. Thus the task of the parent is never really done and is not ended by their children's education, marriage and establishment of a separate household.

3. *Self-recognition of limitations and potentials*

Recognition of one's limitations obviates unnecessary failure, which tends towards depression and discouragement of further efforts. However, limitations should be carefully evaluated so that they may not be used as rationalizations. Rationalizations do possess an element of truth; otherwise they would be delusions. Therefore they should be recognized for what they are—no more, no less. Neither must one's potential be neglected. It has long been known that the potentiating factors involved in our senses tend to diminish their efficiency. Once one of our senses is lost, the other will try to compensate for it. Blindness leads to greater auditory acuity. What is true of our senses is true of many of our other faculties. Medicine deals with augmentation of the potential present in all of our organs, without straining their limitations; thus it is well acquainted with this essential element in mental health.

4. *Adaptability to stress*

This is probably the most important of all the criteria in the assessment of mental health. Adaptability to internal stimuli, the instinctual animistic needs and drives, and to external reality (*i.e.*, society) with its strictures and environment, is the goal of all living matter. A mastery, without renunciation of the instinctual forces within the framework of the reality that surrounds the organism, is the true measure of the mature person. When disbalance in adjustment arises, a pathologic condition ensues. However, the ability to rise above such factors and function despite deficits is the real meaning of health, physical and emotional.

"Health and disease" wrote Nietzsche in his *Will to Power* "be careful! The standard must always be the efflorescence of the body, the resilience, courage and cheerfulness of the spirit—but naturally also *how much morbidity it can absorb and conquer*—in other words, *make healthy*. That which would destroy more delicate men is a stimulant for great healthfulness." Grandiose as this sounds its validity is above reproach.

5. *The human being as an individual*

The emotionally healthy person regards himself and all other human beings as individuals. Although there are character traits common to all people, in that there are common human experiences, the most invariable feature of humans is their variability. It is the variance in the life experience, the different nuances, which dictate a varied approach to oneself and others. This truth compounds the difficulty encountered in the adaptation to people and to treatment. At the same time, however, it multiplies the interest, challenge and creative ingenuity—factors which help engage the intellect of those able and willing to use it, for life and the living.

COMMENT

Except for a constitutional inheritance, one is not born with a specific set of motivations. Motivations for self-realization or the converse are present in all. What one does about them when comparable opportunities are available, is the crucial point. For some people, fortuitous life experiences in an emotionally healthy family create opportunities. The rest of us must continue to work and create our own opportunities to enhance our chance for healthful positive years.

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THE INTEREST OF THE JUNIOR LEAGUES IN AGING PEOPLE*

MRS. ALEXANDER S. PARR†

Association of the Junior Leagues of America, Inc., New York, N. Y.

All of us start to grow older from the moment of birth. It's a shattering thought in one way, as your mind's eye focuses on a tiny baby in a tiny bassinette. And yet we all know it is true: every minute of every day brings us inexorably closer to old age. Science tells us, in fact—if this is any comfort—that we age most rapidly in the first nine months of life. (Have you seen any grey-haired babies lately?)

At the same time, the concept of aging beginning at birth can be a somewhat salutary thought. It places the phase of life known as old age in its proper context.

Childhood. . . . youth . . . . maturity . . . . old age—the cycle of life that has been rolling since the year one.

It has been said, with more than a grain of truth: "We hope to grow old, and yet we dread old age." One of the primary purposes of the American Geriatrics Society is to help ease that dread, or better still, to eliminate it entirely. It is not a simple task, as anyone who has worked in the field well knows. It is something that we of the Junior Leagues have come to learn in the past decade. Of all the many problems involved in aging, the *heart of so many difficulties is dread.*

It is a dread of stiffening bones and failing eyesight, of declining funds and separation from the family. It is most often a dread of loneliness. Horace once wrote: "Waning years steal from us our pleasures, one by one; they have always snatched away my jokes, my loves, my revellings, and my plays." In fact, no matter who he might be, when it comes to the subject of old age, no one seems to have much in the line of joy to say about it—from Plato's "Old age is a dreary solitude" to even the young-in-heart Robert Burns who wrote:

> The fears all, the tears all,
> of dim, declining age.

But those people wrote in the years before wonder drugs, social security, pension plans, medical insurance, retirement travel plans, clinics for the aged, and all the other programs, discoveries and benefits that have lengthened and enriched life far beyond the bouncy and active years. And I must add also, that they wrote in the years before the American Geriatrics Society and before the Junior Leagues first became interested in the problems of aging!

There may be a few here today who wonder what in the world the Junior

* Presented at the 18th Annual Meeting of the American Geriatrics Society, New York, N. Y., June 22–24, 1961.

† Administrator, Association of the Junior Leagues of America, Inc.

Address: The Waldorf-Astoria, New York 22, N. Y.

Leagues have to do with geriatrics; and then, after they've crossed that bridge, wonder what in the world the Junior Leagues might do for aging people. You might be surprised—first, at the depth of our interest, and second, at our record.

Roughly ten years ago, we as a group became actively engaged in gerontology programs. It began on a pilot-study basis, and before long spread into many areas in which the League operates. Our whole program couldn't have taken hold and grown if it wasn't reasonably successful in its modus operandi.

JUNIOR LEAGUE GERONTOLOGY PROGRAMS

You may know that the scope of our work ranges from the rehabilitation of alcoholics to teaching old couples how to bowl. In between these two extremes is a whole world of activity. You might be interested in some of the things we have learned about aging people in our various projects during the past ten years.

Relationships with the aged

Probably the prime lesson we have learned is that the most important factor in our rapport with older people is the soundness of the mutual relationship. We could be involved in the most magnificent and best-equipped Senior Centers from coast-to-coast, we could spend hours on end providing tasty meals; we could read our eyes out or grow hoarse teaching some particular art or craft, and yet all we might do would amount to no more than a thimbleful of water if the relationship between the individual Junior Leaguer and the individual older person was not built on a solid grounding of understanding.

I don't mean a complete case-history understanding. That belongs to the portfolio of the physician or psychiatrist or possibly the professional social worker. But if we are to supplement properly the work of the medical or social expert, we know we must be quite deeply aware of a number of things.

We have found it is very helpful to have a general background knowledge of the kind of life the older person might have led prior to entering a home or hospital, or simply to visiting a Senior Center.

Was the man a robust businessman with many aggressive qualities, or was he a mild-mannered bookkeeper? This might explain, for instance, his present eating habits. The aggressive type constantly complains about the food, when you know it is good food and everyone else is satisfied. On the other hand, the withdrawn type will touch little or no food. Knowing a little of the past history may provide the key for assisting in coping with the current situation.

It is of vital importance to know the older person's relationship with other people, especially his own family. Are there children, and how often do they see them? Are there grandchildren? How many friends do they have about their own age? What is the nature of the relationship—warm and personal, or cool and distant? This kind of knowledge can give all of us the needed background in attempting to ease the aging person's anxiety.

As long as we are human beings, some kind of anxiety will always come into play, no matter who we are or what age we are—another reason for knowing ourselves well before we become too deeply involved with the problems of aging

people. Our main purpose in having this kind of information is that we may develop into knowledgeable assistants who will become aware of the various danger signals, and thus spot things in time to avoid anxieties that grow into fears of the awful kind that can gnaw into an aging person and balloon far out of proportion and perspective.

One of the great and happy solutions for anxiety and fear is work. As someone once said, and so wisely: "Work never killed anyone, but worry has."

Give a person work, and the worries seem to disappear. I don't necessarily mean full-time or part-time employment. If health and strength and mental activity permit, work is the most wonderful solution of all, but we know it is difficult to find gainful employment for people over the age of 65. By work, I mean occupation—meaningful occupation. Occupation to fill the mind and keep the hands busy. Occupation, if possible, that is needed, so that the aging person feels he or she is needed.

No one in the Junior League has ever come across an aging person complaining about a lack of facilities anywhere. They complain only of idleness. A small child wants to help her mother around the house. She feels in her own young mind that she is doing something that is needed (although she may break a cup or two in the process). As we reach maturity, we must do something, whether it is a full-time job or social work or what have you. Without occupation, we are vegetables. There is some unwinding as we reach the riper years, but one basic premise remains; we want to be doing something and, hopefully, something that is worth while.

I'm reminded of an aging woman in Boston who loved to work in her garden producing flowers of the most exotic variety. As the years went by, her interest began to pale. Her zest for living began to dwindle. It was the old routine, and only a handful of people were able to see and appreciate her skill anyway. Then she took up the hobby of making flowers from colored materials, that simulated those grown in the garden. Before a year passed, she had created hundreds of replicas that she sent to hospitals and orphanages. Her new handiwork was seen and appreciated everywhere. A zest for living was revived, and she admitted it was the fact that now she felt she was doing something worth while. Her garden had been a somewhat selfish occupation; her handmade flowers provided a selfless occupation, and it made her very happy. She was satisfying that internal something deep within herself—a key to happiness, we all know, whether we're 8 or 80.

Definition of aims

No matter what the subject matter, it is extremely helpful to begin with definitions. They can clear up a great many obscurities and often set something so definitely into context that we need not fret any more about it. At a psychiatric seminar conducted a few years ago by Dr. Alvin I. Goldfarb, Chief of Neuro-psychiatry of the Home for Aged and Infirm Hebrews of New York, it was pointed out in no uncertain terms that old age is a biologic process found in all living matter that goes through a period of growth, maturity and decline.

Simple and irrevocable, isn't it? "Although we cannot do much about our genes or aging," it was stated, "we can control the environment better, and retard or reduce stresses and disease." That, I suppose, is about the most succinct description you might find to explain the function of the American Geriatrics Society, as well as what we of the Junior League have been trying to do for ten years, and would like to do more of in the coming years. We'd like to help control the environment better, retard or reduce stresses and disease.

During the seminar, Dr. Goldfarb said there was too much anxiety among aging people about the loss of such things as speech and writing capability and other mental functions associated with youth. He thought that re-education should be concentrated on specific functions. "We should try," he said, "to make for the most favorable circumstances . . . the pleasantest possible surroundings . . .to create the best possible emotional atmosphere. . . . to reduce strains and demands on the individual . . . and lead out from past interests to avoid isolation."

Activities

In all of these areas, we of the Junior Leagues have been working with our various gerontology programs. There are now close to 80,000 members in the 199 Leagues. We first began our projects for the aging on a shoestring basis ten years ago. We now participate in, or operate, 44 Senior Centers and Clubs ranging from some of the smallest like that in Boise to the largest like those in Chicago and Detroit. This is only the beginning. We have hopes of doubling the number of Centers in the next decade.

What do we do at these Centers? Our activities are as varied as the situations we come across.

At the Watkins Center in Kansas City, Missouri, for instance, we work with older colored folks. Regular meetings are conducted with prayers, hymns and pot-luck suppers. At another Center in the same city, our volunteers serve coffee, visit, play cards and help with birthday dinners.

At the Senior Citizens' Information Center in San Diego, aging people are given details and advice on housing, jobs, recreation and the many problems that arise as part of getting established as a senior citizen.

In Utica, New York, there is a Senior Day Center—a nonsectarian establishment for older residents of the community, who can come every day during the week except Saturday and Sunday for recreation, training in hobbies, craft work and other free-time interests.

The Wilmington Senior Center in Wilmington, Delaware, was established by the League to help in recreation and companion programs for the increasing number of senior citizens in the community. League volunteers do secretarial work, teach arts and crafts, perform hostess duties and drive older citizens.

In Pittsburgh, the League spearheaded "The Golden Age Hobby Show" for displaying the handiwork of the city's senior citizens. The project was co-sponsored with the *Pittsburgh Press*. League volunteers registered the hobbyists, performed hostess duties, and worked in the shop where the handiwork went on

display; 1,922 people attended the show. One of the goals of the League in Pittsburgh is the establishment of a year-round shop.

In Los Angeles, the League provides hostessing, counseling, and advisory, teaching and organizing programs. Classes are conducted in ceramics, games, special events and the showing of films.

In the Oranges and Short Hills areas of New Jersey, our "Meals on Wheels" program brings food to elderly or disabled persons recommended by hospitals or social workers.

In Boise, League volunteers aid the professional staff in the chronic care of elderly patients in the Geriatrics Ward of St. Alphonsus Hospital.

At the Mary Pomeroy Green Senior Center in Chicago, monthly parties are held which are planned by the League. A second Senior Center opened in 1959 in a Chicago Public Housing unit, and a third Center is in the planning stage.

In Newburgh, New York, League volunteers have a program in operation in which twelve girls each month drive Senior Citizens to Salvation Army headquarters—about the only time these older people manage to get out in the fresh air.

These are but some of the highlights of our activities. I mention them only to give you a clearer idea of what we do specifically across the country to give a lift to aging groups. There may be a few of you here today with the image of the Junior League as a organization of flighty young dames lost amidst the tinkle of tea cups. Well, keep thinking of us as young dames; we don't mind that a bit. But if there is any one impression I should like to leave with you, it is that we are deeply interested in the same thing you are interested in—doing what we can to ease the stress and remove the dread of old age.

STATISTICS

Obviously, your burden is not going to lessen in the years ahead. You probably saw the recent analysis of the U. S. Census Bureau report made by the Senate Special Committee on Aging, pointing out in black and white that in the United States there are nearly twice as many persons 65 years of age or older than there were in 1900. It also emphasized the fact that the elderly, as well as the young, are living longer.

In 1900, only 1 of every 20 Americans had reached 65 years of age. Today 1 of every 11 is 65 years or older. The data gathered by the Census Bureau made it clear beyond a doubt that reduction of the death rate among infants and children was not solely responsible. Medical and social progress is lengthening the lives of the aged, just as in earlier years it lengthened the lives of the young. In the decade between 1950 and 1960, there were each year (on the average) 426,488 additional persons aged 65 and over, compared with each previous year. And only a slight percentage of this total can be accounted for by immigration.

Today in the United States there are more than 16.5 million persons 65 and older. This is an increase of more than 11.5 million over the numbers in the same age group in 1920.

"The 236 per cent increase in the number of persons 65 years and older and

the 279 per cent increase of those 75 years and older in the 40 years between 1920 and 1960 is extraordinary," the report states. "The 920 per cent increase in those 85 years and older is phenomenal." Obviously, you ladies and gentlemen of the American Geriatrics Society will not be running out of subject matter in the near future!

The prediction for the coming forty years is for a total of 30 million persons 65 years and older in the United States. Dr. Herbert S. Robb of the Wayne College of Medicine has calculated that if atherosclerosis and cancer were cured, the ordinary life span might be 120 to 130 years. So, folks, we haven't even reached the mid-point yet!

COMMON GOALS

You have your work cut out for you, and it's going to do nothing but increase in the years ahead. We of the Junior League are here to help in any way we can. Are you taking advantage of us?

We have a number of goals in common, and the prime goal for both our groups is the same—the eventual removal of *dread* in association with the ripe years.

In your study and work with the aging, you must certainly run across a number of humorous items and anecdotes. You may get a chuckle from this one I heard a long time ago. It really points up what great things can happen when some of the frivolities of youth pass into the solidities of old age:

King Solomon and King David
Led very merry lives,
With very merry concubines
And very many wives,
Until old age came creeping,
With very many qualms,
Then Solomon wrote the Proverbs,
And David wrote the Psalms.

PSYCHIATRIC EVALUATION OF A CHRONICALLY ILL GERIATRIC HOSPITAL POPULATION

H. GRAUER, M.D.* AND M. STRAKER, M.D., F.A.P.A.†

Jewish Hospital of Hope, Montreal, Quebec, Canada

Patients suffering from a psychiatric illness are often admitted to other than psychiatric hospitals. They may be treated or institutionalized in county homes, homes for the aged, nursing homes, hospitals for the chronically ill and in correctional institutions. In settings such as these, their "mental illness" as such often goes unnoticed, even if it is treated symptomatically. The purpose of this paper is to report a psychiatric survey carried out at a hospital for the chronically ill—the Jewish Hospital of Hope in Montreal, Canada.

Very few studies of this type have appeared in the literature in the recent past. Ginzberg and Brinegar (1) surveyed the population of a county home in Iowa. They studied 87 men and 39 women (mean age, 75.2 years), and reported that 39.2 per cent were psychotic, 17.7 per cent were mildly mentally ill or neurotic, and 3.9 per cent could not be classified; 36.2 per cent did not suffer from a psychiatric disorder. Another study in which a chronically ill geriatric group was psychiatrically evaluated was carried out by Friedfeld *et al.* (2). Here a geriatric clinic population was studied. In a group of 100 patients, 83 per cent were neurotic, 11 per cent were psychotic, 10 per cent were disoriented, and 18 per cent suffered from pronounced memory disturbances.

The aim of our survey was twofold: 1) to assess the psychiatric problems at the hospital, and 2) to evaluate admission procedures, which up to now have excluded mentally ill patients.

The institution at which the study was undertaken is a nonsectarian, 115-bed hospital for the chronically ill and aged. It is staffed by 3 full-time physicians, as well as nurses, physiotherapists and other auxiliary personnel; it also has a large consulting staff, with all major medical specialties being well represented. Patients are mostly confined to bed or a wheelchair; the majority, however, are able to look after their immediate needs. Patients are admitted from their homes or transferred from active treatment hospitals in the Montreal area. Each patient prior to admission is screened by a member of the hospital staff.

METHOD OF STUDY

The study was carried out over a period of one year. Both the existing hospital population and all new patients admitted during that time underwent an evaluation which included: 1) a review of the patient's hospital chart including discharge summaries of previous hospitalizations; 2) an appraisal of the patient obtained from consultation with the hospital staff; 3) an interview, when possbile,

* Clinical Assistant Psychiatrist.

Address: 900 Sherbrooke Street West (Suite 14), Montreal, Quebec, Canada.

† Psychiatrist.

with the patient's relatives; and 4) a psychiatric examination, including a psychiatric history and a mental status examination. All psychiatric examinations were made by one of the authors (H. G.). The mental status examination evaluated orientation, recent and remote memory, retention and recall, mood and affect. Hallucinations and delusions were noted when present. The psychiatric examination was occasionally made difficult by motor or sensory aphasia. In these cases a blackboard and calendar were used to facilitate the examination.

CLINICAL DATA

Of the 113 patients examined, 51 were men and 62 were women. Fifteen patients were single, 44 were married, 45 widowed and 9 separated or divorced (Table 1). The average age was 64 years. The age distribution by sex is shown in Table 2.

Fourteen of the 113 patients had a previous psychiatric history. Some of them had been previously treated by a psychiatrist; others had undergone psychiatric hospitalization.

Orientation was judged on the basis of the patient's response to questions regarding person, place and time. Of the 113 patients interviewed, 40 were found

TABLE 1

Marital Status, by Sex

Marital Status	Male	Female	Total
Single	4	11	15
Married	26	18	44
Separated or divorced	8	1	9
Widowed	13	32	45
Totals	51	62	113

TABLE 2

Ages of the 113 Patients, by Sex

Age (yrs.)	Male	Female	Total
20–29	0	1	1
30–39	1	2	3
40–49	3	2	5
50–59	9	10	19
60–69	11	17	28
70–79	18	17	35
80–89	8	12	20
90–99	1	0	1
100–110	0	1	1
(mean age, 64) Totals	51	62	113

to be properly oriented with respect to all three factors; 41 were partially oriented, and 32 were completely disoriented (Table 3). Further in the sensorial examination, it was found that 2 patients suffered from auditory hallucinations, and 9 from delusions. In evaluation of the mood, 27 patients were depressed and 6 were euphoric. The affect in 1 chronic schizophrenic patient was described as "flat"; in 12 other patients it was described as "labile."

Diagnosis. When applicable, a psychiatric diagnosis was made. For only 11 patients had a psychiatric diagnosis been officially charted. This usually concurred with the diagnosis made by the authors. Of the 113 patients seen, all but 11 had a psychiatric disorder. The official American Psychiatric Association classification was used (Table 4). Table 5 shows the etiologic distribution in the chronic brain syndrome group.

Treatment. The protective milieu, the treatment of the associated physical disease, and both occupational and recreational therapy programs are extremely important in psychiatric treatment. However, it is simpler to evaluate treatment on the basis of the amount of psycholeptic and psychoanaleptic drugs used. These drugs were given to 82 per cent of the women as compared with 53 per cent of the men (Table 6). The psycholeptic therapy was classified into night and day-

TABLE 3

Orientation, by Sex

Orientation	Male	Female	Total
Complete	22	19	40
Partial	15	26	41
None	14	17	32
Totals	51	62	113

TABLE 4

Psychiatric Diagnoses

I. *Chronic brain syndrome:* mild	18		
moderate	31	87	
severe	38		
II. *Depression, reactive:* chronic	6		
acute	1	7	
III. *Passive dependent personality disorder*		4	
IV. *Schizophrenic reaction:* chronic		1	
V. *Mental deficiency;* with psychosis	1		
without psychosis	1	2	
VI. *Conversion reaction*		1	
VII. No psychiatric diagnosis		11	
Total		113	

TABLE 5

Causes of Chronic Brain Syndrome: Underlying Pathologic Processes

1. Multiple sclerosis	3
2. Intoxication	1
3. Senile atrophy	1
4. Amyotrophic lateral sclerosis	1
5. Cerebral palsy	1
6. Infection	3
7. Circulatory disturbance	77
Total	87

TABLE 6

Treatment with Analeptic or Psycholeptic Drugs

Drug	Men	Women
Analeptics	2	4
Psycholeptics: night	15	18
day	9	17
both	2	16
Totals	28	55

time sedation. Fifteen men received night sedation; 9, daytime sedation; and 2, both. Eighteen women received night sedation; 17, daytime sedation; and 16, both. Two men and 4 women were treated with analeptics (Table 6).

DISCUSSION

The most important single finding in this survey was that 90 per cent of the patients suffered from a diagnosable psychiatric illness. Conversely, for only 11 patients (or 10 per cent of the total population of the hospital) was a psychiatric diagnosis officially charted. In trying to assess the patients' contact with reality—one of the criteria used in establishing whether or not psychosis is present—we found that over two-thirds of the group were completely or partially disoriented; 60 per cent of the male patients, and 69 per cent of the female patients were not sure of the time, place or person.

Seventy per cent of the patients received sedative drugs to reduce psychomotor activity during the day and/or to induce sleep at night. Thus, so far as treatment was concerned, there was an awareness of the psychiatric and psychosomatic problems. By the use of neuroleptic drugs, disturbed, confused and disoriented patients can often be adequately handled in an open setting.

CONCLUSIONS

Although, at the present time criteria for admission to this hospital exclude psychotic patients, a more realistic approach would be to admit all chronically ill patients, as long as they do not exhibit behavior which would make them

dangerous to themselves or others. Each patient should continue to undergo periodic psychiatric assessment, for both diagnostic and therapeutic purposes. Should the patient become a behavior problem, arrangements can always be made for transfer to a psychiatric institution. The patients' relatives should be made aware of this stipulation prior to admission.

Above all, there is a need for close cooperation between the hospital staff and the attending psychiatrists, since only in this way can the chronically ill patient receive the comprehensive care he needs.

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POSTMENOPAUSAL OSTEOPOROSIS: A DISTURBANCE IN OSTEOCLASIA*

H. M. FROST, M.D.

Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, Michigan

The purpose of this paper is to summarize the evidence indicating that postmenopausal osteoporosis is the result of a disturbance in osteoclastic, rather than osteoblastic activity. Terms should be defined first, however, so that reader and writer are thinking of the same thing. There is a great deal of semantic confusion in the literature on metabolic bone disease, and this partly accounts for the current conceptual confusion and misinformation in this field.

DEFINITION OF TERMS

Osteoporosis. A decrease in the total amount of bone in the skeleton (1–4). The amount is best expressed volumetrically, as pointed out by Robinson and Elliott (5) and the writer (6). The quality of osteoporotic bone need not be normal; this is a separate story.

Postmenopausal osteoporosis. The osteoporosis seen in women after cessation of the menses. The menopause may have been spontaneous or iatrogenic. As pointed out by Nicolaysen *et al.* (7), Nordin (8, 9) and Smith *et al.* (10), many other factors are involved in this form of osteoporosis, such as dietary insufficiency of calcium (11) and protein, body types and racial derivation. For the present purpose, postmenopausal osteoporosis and senile osteoporosis are separated, although there is little justification for the assumption that they are separate diseases.

Osteoblastic activity. The amount of bone formed in the skeleton per unit of time. This new bone is formed by osteoblasts, and the steps in its formation are complex. The total amount of bone formed in the skeleton per unit of time is the total product of the manufacturing effort of all the osteoblasts, and thus is a valid measure of their activity. Osteoblasts form the organic bone matrix. This matrix subsequently is mineralized, whereupon by convention the whole is termed bone (1, 4, 12–14).

Osteoclastic activity. The amount of bone resorbed in the skeleton per unit of time. It is the opposite of osteoblastic activity. The total amount of bone present in the skeleton at any one time is the result of the state of balance between bone formation and bone resorption in the total time prior to the moment of observation (Fig. 1). It is assumed that bone is resorbed *in vivo* only by cells designated as osteoclasts (6, 14, 15), and that bone does not mysteriously disappear through the operation of another *in vivo* mechanism. There is excellent justification for this statement (16).

Protein anabolic hormone theory of osteoblastic control. According to this theory,

* Work aided by the following grants: #293 HFH; A-4186 NIH.; Orthopaedic Research Education Foundation.

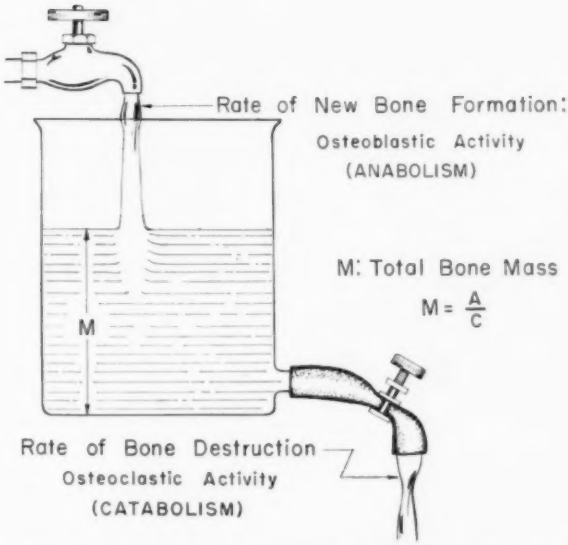

FIG. 1 Schematic representation of the concept of skeletal balance. The amount of fluid in the vessel at any one moment represents the amount of bone in the skeleton at any one moment. On the basis of an average density of 2.2, and an average skeletal mass (dried, degreased, bleached) of 2.8 Kg., the average volume of bone in an adult human skeleton is 1.3 liters. Marrow spaces, vascular channels, lacunae and canaliculae are not included in this estimate.

The amount of fluid in the vessel is dependent upon the balance between the rate of inflow and the rate of outflow over a previous time-period. A decrease in fluid represents osteoporosis. A number of different alterations in rates may lead to negative skeletal balance and osteoporosis. (Reprinted by permission from Frost, H.M.: Osteoporosis: the orientation of future basic research, *Henry Ford Hosp. Med. Bull.* **9:** 183, 1961.)

the protein anabolic hormones (particularly estrogen) exercise important homeostatic control over osteoblastic activity; thus osteoblasts are stimulated by estrogen to produce more organic bone matrix. It also held that after the menopause, as well as in the senile patient, the drop in secretion of the endogenous anabolic hormone leads to a decrease in the amount of organic bone matrix formed by the osteoblasts (17, 18). In view of the undisturbed bone resorption, this state of affairs would lead to osteoporosis as defined here.

OBSERVATIONS

Influence of estrogen in osteoblastic activity

If osteoblastic activity were governed to a significant degree by estrogen, then in the majority of *all* postmenopausal women not only would some degree of osteoporosis develop (which, in fact, is the case), but the cause of this development would be a decrease in osteoblastic activity. Up until three years ago the difficulties in measuring human osteoblastic activity were so great that no conclusive statement could be made regarding this activity, despite numerous and ingenious attempts to crack the problem. The situation is now altered by the following studies:

(*a*) Human osteoblastic activity was measured (13, 19) in a series of ribs and

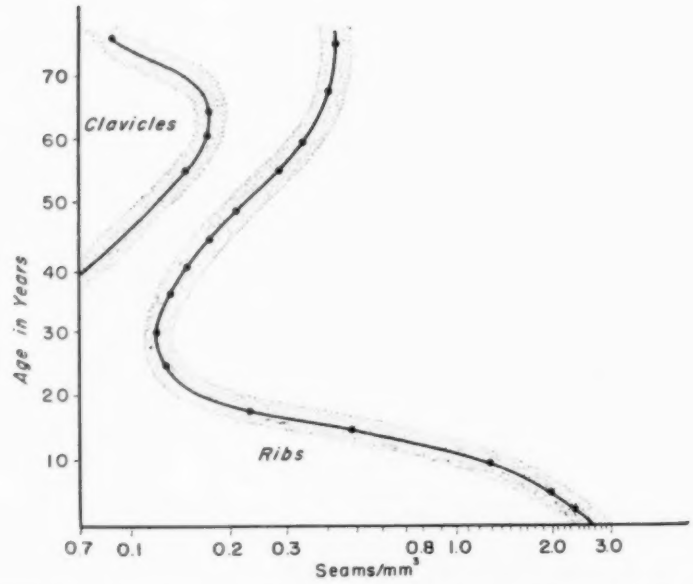

FIG. 2. A curve of the relationship between age and lamellar osteoblastic activity in the cortex of the human rib (65 cases) and clavicle (35 cases). The smoothness of the curve is artificial and is due to the method of calculating the mean values. The relative values by age are significant, however.

Note that after age 30, when the body's endogenous supply of protein anabolic hormones is *decreasing*, the measured osteoblastic activity is *increasing*. Any effect of these hormones on osteoblasts must be insignificant. (Reprinted by permission from Frost, H. M. and Vilanueva, A. R.: Human osteoblastic activity, I., *Henry Ford Hosp. Med. Bull.* **9:** 76, 1961.)

clavicles in terms of the number of bone-forming centers per unit volume (osteoid seams per cu. mm.), and the unexpected but unequivocal answer was that osteoblastic activity at age 55 is *double* that at age 30 (Fig. 2). Thus, at an age when the protein anabolic hormone theory would predict a decline in osteoblastic activity, actual measurement revealed an increase.

(*b*) The amount of new bone formed in a unit volume of the skeleton in a unit time was measured (20) through the use of human bone labelled with tetracyclines. The initial report by Milch, Rall and Tobie (21) that the tetracycline antibiotics become fixed in new mineralizing bone in much the same fashion as alizarin, has stimulated a great deal of physiologic research on the skeleton. The tetracyclines label new bone; if it is lamellar rather than fibrous, it appears like growth rings in undecalcified cross sections of the long bones. By the use of simple microscopic, planimetric methods it is possible to measure the amount of bone labelled by the tetracyclines. If the time period over which the tetracyclines were administered is known, then a true measurement of the amount of bone formed per unit volume of the skeleton per unit of time becomes possible (16) (Fig. 3). Such a study has been made in 28 human subjects, and the results (20) corroborate the validity of the measurements summarized in the foregoing section (*a*).

FIG. 3. Undecalcified cross-section of human femur. The patient had received tetracycline antibiotics three years prior to amputation for a sarcoma of the leg. This photomicrograph was taken in blue light fluorescence.

The white areas are bone labelled with tetracycline. This bone was being formed during the time the tetracyclines were being administered. In cases in which the duration of this time is known, it is possible to obtain a true measurement of bone formation in properly prepared sections.

(*c*) One of the patients in the tetracycline study of section (*b*) had severe postmenopausal osteoporosis untreated by hormones, yet osteoblastic activity was the highest in her age group. Moreover, work with radioisotopes in patients with osteoporosis has indicated that there is no retardation of osteoblastic activity in these cases (8).

Influence of estrogen on new bone formation

The notion that estrogen stimulates the formation of new bone is so deeply ingrained in current medical literature that it is profitable to review its origin, and to compare the findings with those of modern basic investigative work.

(*a*) Initially it was noted that, in some birds prior to mineralization of the egg shell and in mice prior to lactation, an increased amount of bone appeared in the metaphyses. It was proved that estrogen was the major factor involved in this increase of bone. From this point on, events took two divergent courses: 1) speculation that a deficit of estrogen was the cause of postmenopausal osteoporosis, and prompt utilization of estrogen for the treatment of this disorder—a concept maintained by a small but vociferous group of investigators ever since; and 2) serious disagreement with the foregoing concept on the part of a rela-

tively mute group of investigators who have been ignored for the most part since they could not replace this idea with a better one.

(*b*) Day and Follis (22) belong to the second group; in 1941 they published one of the best studies on the effects of estrogen on the skeleton of the mouse. They observed that the increased amount of new bone found in the diaphyses of these mice appeared to be the result of a decrease in osteoclasia rather than (or as much as) an increase in the rate of new bone formation. They also pointed out that the new bone present under the epiphyseal plate in mice after treatment with estrogen was fibrous, and there was no significant increase in the amount of new bone in the diaphyses of treated mice. The latter observation is significant, since it is in the diaphyses that lamellar bone formation would be prominent in growing mice. Near the epiphyses of growing animals of any species, fibrous bone formation predominates or else there is an unpatterned mixture of fibrous and lamellar bone formation.

The results of Day and Follis have since been duplicated by others, notably Budy, Urist and McLean (23, 24). Although these studies may be criticized on the grounds that the quantitative histologic data were not very reliable, this objection applies equally to investigators who adopted the opposite view (namely, that estrogen stimulates increased bone formation). As will become evident, the latter zealous group saw too much. As long as they rode on the crest of the wave of estrogen popularity, it was difficult to present a dissenting view.

(*c*) Radioisotopes have proved a powerful tool for physiologic investigation since their increased availability following World War II. Many studies of skeletal uptake and release of boneseeking radioisotopes have been made in the last fifteen years. Allowing for early confusion about methods and interpretation, the studies of the past five years are particularly pertinent to the present theme. An example is the excellent study recently reported by Cordrey, Christie, MacIntyre and Palmer (25). These investigators used strontium^{85} and measured its uptake and release by the skeleton in castrated and in uncastrated mice. Their data show that the presence of estrogen in the body decreases the release of the skeletally deposited isotope to the blood, whereas the absence of the hormone increases this release. They concluded that their data could not be understood on the basis of then-known facts. It is clear now that the estrogen affected primarily the osteoclastic activity in these animals. When viewed in this light, the data are not only perfectly comprehensible but are also quite consistent.

Lamellar and fibrous bone

The various human osteoporoses are diseases of *lamellar* bone. The bone present in increased amounts in estrogenized birds and mice is *fibrous*. If one wishes to understand skeletal physiology and pathophysiology, the concepts of lamellar and fibrous bone and of lamellar osteoblastic and fibrous osteoblastic activities must be mastered (12). These two types of bone are formed by cells subject to different controls, or responding differently to the same controls. Accordingly it is not only impermissible but erroneous to assume that what affects fibrous bone will similarly affect lamellar bone. Ignorance of this simple

fact has given rise to much confusion and many misstatements concerning the pathology of osteoporosis.

This problem will be restated so that the reader will be in no doubt of our stand in the matter. The adult skeleton is composed almost entirely of lamellar bone (1, 4, 12); the osteoporosis of adults is the result of a disturbance in the balance between formation and resorption of lamellar bone (1, 2, 4, 14, 26); and the cells forming lamellar bone are governed as to rate and quantity by different factors or to different degrees than are the cells forming fibrous bone (12).

Fibrous bone is the reactive bone found in fracture callus, in the walling off of various skeletal irritative lesions, just under the epiphyseal plate in growing animals, and in the excess metaphyseal bone formed in certain animals and birds treated with estrogens (12, 14). Whatever may be the vagaries of fibrous bone formation in animals under the influence of estrogen and other hormones (27), these vagaries do not affect the cells forming lamellar bone in humans to any significant degree.

Method for measuring new lamellar bone

A quantitative, self-controlled, tetracycline-based method for measuring the rate and quantity of new lamellar bone formation under controlled experimental conditions has been evolved in this laboratory.[1] Results of studies with this method indicate that, in rats at least, estrogen has no measurable effect on lamellar osteoblastic activity (16).

Method for measuring osteoclastic activity

A qualitative method for measuring osteoclastic activity has revealed that in a group of 12 osteoporotic patients the osteoclastic activity was about 4 times greater than in a group of normal subjects (16). This finding is significant because, if osteoblastic activity is increased after age 30, the only way osteoporosis could develop would be as the result of a proportionately larger increase in osteoclastic activity. The behavior of osteoblastic activity was the phenomenon that led to this study in the first place.

DISCUSSION AND SUMMARY

There is no valid evidence for the belief that estrogens stimulate the formation of new lamellar bone in animals or in humans.

There is no compelling evidence for the belief that estrogens stimulate the formation of fibrous bone in animals. Administration of estrogen results in an increase of fibrous bone, apparently brought about by retardation of osteoclastic activity; this is quite a different process from stimulation of osteoblastic activity. Failure to distinguish histologically between fibrous and lamellar bone formation has created vast confusion about the nature of osteoporosis, its causes, and the factors governing osteoblastic activity in animals and in man.

The available evidence, both direct and indirect, supports the thesis that

[1] Henry Ford Hospital Orthopaedic Research Laboratory

postmenopausal osteoporosis is a disorder of osteoclastic activity. The cause of the increase in osteoclastic activity in this disease is unknown.

Research on postmenopausal osteoporosis needs re-appraisal. The *nature* of the affected bone, and the factors that control *osteoclastic activity* must be identified and studied before effective therapeutic programs can be formulated.

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ORTHOPEDIC PROBLEMS OF AGING

BRADFORD S. BENNETT, M.D.*

Winchester, Virginia

The orthopedic problems of aging are manifold. They involve the supporting tissues of the bones and joints—synovia, joint capsules, ligamentous attachments and muscle-nerve units—as well as the structures themselves. A wealth of knowledge obtainable only through team approach to individual and mass investigation is necessary in order to make sound decisions leading to rational treatment. The orthopedist should contribute heavily to the proper assessment of these situations so that the result will be corrective and prophylactic habilitation of the individual or group. The orthopedist is in a unique position compared to that of any other specialist, excluding perhaps the pathologist, oculist and dentist. He sees and treats the patient from birth (in cases of congenital developmental and traumatic conditions) to senescence (in cases of degenerative processes). He watches bone growth and development. The changing function and maturity of the supporting structures of the musculoskeletal system are constantly in his view. Associated with the orthopedic changes in the aging person are changes in the neuromuscular and central nervous systems. These conditions, if not the cause of the pathologic change, are significant enough to be considered and treated.

FASCIITIS AND FIBROSITIS: MUSCLE SPASM

In the musculoskeletal system, the hands alone give rise to many disabling problems. The older person who has worked hard all his life may be plagued with palmar fasciitis or Depuytren's fibrosis. Relief can be provided by rather extentive or even limited surgery, using local anesthesia for excision of the nodules and fibrous bands. The trigger-finger phenomenon due to nodules on the flexor tendons or to constricting bands of fibrous tissue is easily cured by surgery under local infiltration anesthesia or local nerve block. Spontaneous rupture of tendons, such as the extensor tendons to the thumb and fingers, requires only a simple procedure; general anesthesia is necessary, however. Early ambulation and activity are very important factors in recovery. For the residual effects of arthritis, surgical procedures such as capsulotomy or arthroplasty of the fingers are satisfactory. Older people are anxious for recovery, and in selected cases much can be accomplished.

Procaine treatment of muscle spasm. Local anesthetic agents, such as procaine, are very effective when injected into "trigger" areas. For example, in a patient with a "stitch" in the back, one will find some local areas more sensitive than others, usually in association with rather marked muscle spasm. Gentle massage and infrared therapy, the time-honored approach in many clinics, may be ineffective. If so, immediate relief may be obtained by local infiltration of the painful

* *Address:* 214 W. Boscawen Street, Winchester, Virginia.

trigger area; the anesthetic agent is then fanned out in the adjoining tissues radially. Gradually, under the relief afforded by the local anesthetic, the patient is able to carry through the normal range of motion of the joints involved. This helps to stretch contracted supporting structures about these joints. Cracking or snapping sounds should be avoided, as they indicate rupture of supporting structures. Mild tearing of fibrous adhesions is to be expected, but not the rupture of normal anatomic structures. When ischemic spastic muscle recovers its normal blood supply and resumes normal tone, the mobility of the associated joints often increases. Nourishment of the inert collagen structures supporting the joints involves action of the muscles. Elasticity is re-established and fluid is restored to the cap of articular hyaline cartilage. Exchange of metabolites is enhanced, thus helping to prevent degeneration of the cartilage. Since the pressure changes induced by muscular action are beneficial to the synovia and cartilage of the joint, any relief of pain in a trigger area sets up a train of relaxation of muscle spasm, re-establishment of adequate circulation and acceleration in the exchange of metabolic products. The intervals between injections of the anesthetic agent lengthen as motion in the joint improves.

Differential diagnosis. Tuberculosis of the wrist and hand in older orthopedic patients can mimick smouldering rheumatoid synovitis or osteoarthritis. Also to be kept in mind are Boeck's sarcoid, burned-out gonorrhea or syphilis, brucellosis, or a disease of metabolism. In the latter category is gouty arthritis. (Debridement of the gouty nodules from the tendons and synovial structures under local anesthesia provides great relief; local injections of hydrocortisone or prednisolone are also helpful.) Rarer conditions are the lesions associated with diabetes, leukemia, pernicious anemia and sickle-cell anemia.

TRAUMA—FRACTURES

Trauma is one of the most common causes of orthopedic conditions. Why do these accidents occur? On investigation one usually finds a history such as this: Grandfather arose at 5 a. m. to go to the bathroom, became confused, and fell to the floor in such a manner as to fracture his hip. We need an educational approach to the prevention of this one type of injury, similar to that employed by the highway department for the prevention of automobile accidents. The latter are called crashes instead of accidents, in order to educate the public to the fact that carelessness or negligence was involved. Most fractures in the elderly are also crashes, not accidents. Carelessness, thoughtlessness, and negligence are implicated in this orthopedic problem of aging.

A major contributing factor is arteriosclerosis. In the old person, oxygenation of the vital centers is perhaps retarded. A change of posture from horizontal to erect may be accompanied by giddiness, temporary loss of balance, confusion and incoordination of gait. Because of urinary difficulties, the patient may have to visit the toilet in the early hours of the morning. Preventive measures include restriction of fluids after supper, control of minor urinary disturbances, and administration of bladder sedatives as indicated. Bed rails, although insulting to the patient when used without explanation, may be life-saving. Waxed floors

and loose scatter rugs should be eliminated. Rails at the commode and in the bathtub area are helpful, as are night lights along the floor boards and in the corridors.

OTHER DISORDERS OF BONE

Parathyroid disease, Paget's disease, or malignant tumors of bone (either primary or metastatic) may cause pathologic fractures. Unexplained generalized osteoporosis of the skeletal system may be present. These conditions call for data on calcium, creatinine, total protein, protein fractions and Bence-Jones protein, as well as a roentgenographic survey. If indicated, detailed calcium, phosphorus and phosphatase determinations are made.

Some understanding of *calcium-phosphorus balance* in normal persons is a prerequisite to understanding disorders of bone in the aged. Much of the relationship is based on the laws of supply-and-demand. Inactivity causes loss of protein substance and a breakdown of calcium proteinate, leading to stone formation and possible osteoporosis. Administration of cortisone upsets calcium balance and bone formation, perhaps through blocking the effect of vitamin D. Calcium increases the movement of citrate from cells to the extracellar fluid. Vitamin D influences the movement of calcium across membranes such as those in the gastro-intestinal tract. The plasma calcium level is the best regulated of all systems; it is buffered by a calcium pool in the bone as well as by blood buffers. Cortisone therapy is further contraindicated because of the poor quality of the granulation tissue formed. Bone repair actually is delayed. Without cortisone therapy, calcium balance can be maintained by increased calcium intake. The patient must be kept active in order to avoid the osteoporosis of immobilization —the atrophy of disuse. Sex hormones can restore calcium-phosphorus-nitrogen metabolism to a positive rather than a negative balance. A quick initial estimate of the patient's metabolic status may be obtained by determination of the calcium-creatinine ratio in a 24-hour urine specimen. If the ratio is greater than 0.28, a negative balance is said to be present.

Malignant tumors of bone become more common with aging. Multiple myeloma, and metastatic malignant lesions from the prostate, kidney, breast and gastro-intestinal cancer are often first manifested clinically in the form of an orthopedic complaint. Retrospectroscopes are valuable devices but do not afford much consolation when one finds he has been treating a backache as arthritis when actually it is due to a metastasis to the sacrum from a gastro-intestinal tumor.

DEGENERATIVE DISEASE OF THE JOINTS

Degenerative joint disease presents another great problem. Dysfunction of the joints due to ordinary wear and tear is well tolerated by most people. The ensuing limitations have usually occurred gradually, so that adaptations to the work environment have taken place. For example, in some disorders of the neck, shoulder girdle and dorsal spine there are periods of acute severe disabling pain, but the pain can be relieved by simple measures and the acutely painful period is usually short. Limitation of the finely coordinated motions of the finger joints

is an emotional and physical handicap to the patient. Dysfunctions of the weight-bearing joints such as the hip, knee and ankle are the prime problem; they can cause the greatest loss of personal dignity and self-esteem if the patient has to remain completely dependent upon others.

Loss of elasticity of the ligaments and tendons is a characteristic of aging. This is associated with loss of viable articular cartilage and its eventual thinning and disappearance. Reactive bone formation (spurring at the joint margins, with condensation of bone and narrowed joint spaces) progresses. As mobility disappears, muscle substance is lost, there is further fibrous replacement in the proximal and distal ends of the fibers, and the overlying fascia becomes bound down. Thus motion is restricted.

There are two forms of this disorder:

1. In association with arthritis. The spine is involved primarily, and the condition is severe. The lumbosacral and fascia lata structures tighten. On palpation they present hard resistant masses, and the sharp edges of the tensor fascia can be outlined through the skin and subcutaneous tissues. Loss of blood supply starts a vicious cycle. Extreme effort is required for the patient to get in or out of a chair, as these movements involve use of the lumbosacral, gluteal, and fascia lata structures. The patient says he is worse in the mornings, being too stiff to move about until he sits in the bath tub or takes a shower. Simple fasciotomy permits increased freedom of motion in the back, hip and knee. Manipulation under light anesthesia followed by mucle relaxants and physical therapy also brings good results. *2.* In association with fibrositis. There is evidence of inflammation with localized "trigger" areas, and slight fever. The erythrocyte sedimentation rate is usually not elevated. Bouts of extreme disability last from a few days to several weeks. Peripheral nerve involvement may confuse the diagnostic picture. The condition has many names. During the last war it was called Guinea back, and there was great discrepancy between the physical findings, and the amount of subjective disability. There is no specific treatment, but many supportive ones. Painful trigger areas do respond to injections of procaine or other local anesthetics.

RESIDUAL EFFECTS OF NEUROLOGIC DISEASE

Cerebrovascular accidents are the prime source of these residual effects. The patient comes to the orthopedic service with a severely contracted elbow, wrist and fingers in the upper extremity and perhaps foot drop, a contracted heel cord, and clonus of the ankle in the lower extremity. Best results are obtained if the patients are treated early in the course of the disease. In cases of poliomyelitis the pediatrician is now so alert to the complexities of the disease that he calls the orthopedist promptly with a view to prevention of undue disability and for early restoration of function. Among other neurologic disease states having orthopedic significance are transverse myelitis, meningitis and multiple sclerosis.

GENERAL ASPECTS OF TREATMENT

Treatment of orthopedic problems of aging acknowledges certain generalities and then specific courses of action for each disorder. The anxiety syndrome is not

uncommon in geriatric patients, either as a condition per se or in combination with organic disease, and improper diagnosis can engender invalidism. Memory impairment is a problem, though the aged patient usually makes a conscientious effort to concentrate and remain rational and articulate. Therefore a central nervous system survey is necessary. Any orthopedic condition requiring hospitalization and surgery puts the aged person on the defensive; no doubt he is more conscious of the clock ticking away his life than is the younger person. The prospect of a stay in the hospital of three months or more is frightening; it represents a proportionately larger share of the remaining years of freedom for an old person than for a young person. Therefore any surgical treatment must be considered in the light of whether it is a goal in itself or whether it will lead to other procedures. Results should be promptly apparent. An example of such considerations would be decision to use arthroplasty in the treatment of a joint lesion, when peripheral neurectomy, or release of the tendons and physical therapy would afford sufficient relief to make the patient comfortable and ambulatory.

Many aged patients show the effect of improper diet. They are anemic, hypoproteinemic, and in a state of negative calcium balance. Perhaps electrolyte balance is disturbed, and there are no defenses against shock or infection because the patient has been receiving steroid therapy. The latter is a serious problem requiring continuous pre- and postoperative medical care. For these reasons the value of an adequate history can not be emphasized too greatly. Any procedure of a surgical nature requires consultation with the anesthetist concerning not only the anesthesia but also such factors as oxygen therapy and fluid balance. Phlebitis as a surgical complication is less infrequent in the older age groups, but the incidence of fibrillation and cardiac insufficiency precludes the use of any anesthetic that would induce anoxia during administration. I recently had a patient in whom paroxysmal auricular tachycardia developed forty-eight hours postoperatively. I should have been warned of this on the basis of her cardiac history, *viz*, unprovoked periods of rapid heart beat, suffocation and an uneasy feeling. The response to quinidine was rapid and satisfactory.

REHABILITATION

The common goal in treatment of the orthopedic disorders of the aged is the rehabilitation of the patient. This problem is the greatest one with which we are confronted. Contributing factors are the shift from rural to urban, and now to suburban concentrations of our people; our increased longevity; the cigar-box type of present-day housing, not built to accommodate an aged relative; and such incidents as the crises engendered for in-laws by the unexpected recovery of grandaddy from his injury or illness. The interest of the state, community and federal government also contribute to the complexity of the problem.

Any definitive surgical procedure for treatment of the residuals of trauma is evaluated differently today compared with ten years ago. It is now realized that a procedure involving twelve to sixteen weeks for recovery with questionable functional improvement is something not to be taken lightly by an old person, as

it represents a large proportion of his life expectancy. Therefore surgical judgment in these matters is of the utmost importance. Procedures affording relief of pain have to be evaluated against procedures that correct the dysfunction. Older people learn to live with a functional disability. However, they want not only improved function of all body activities but, much more, freedom from pain.

CONCLUSIONS

The orthopedist should weigh the patient's personality, environment and physical reserve in planning a course or action. First of all, the patient should be convinced that an active step has been taken toward his rehabilitation once the surgical procedure has been performed. He should not have to wait for the "laying on of hands" until his discharge from the orthopedic ward or at the time of removal of the cast or other corrective apparatus. When a patient is bedridden in the hospital or in his home, insidious changes such as a decrease in coordinative ability, loss of muscle tone, formation of kidney stones, and mental stagnation with confusion and disorientation, are accelerated. All of these factors are the concern of the orthopedist. Treatment is facilitated by the team approach involving trained personnel who confer with the patient, the nurse, the doctor, the family and the employer. Such trained personnel include the social worker, the clergyman, the occupational therapist, the physical therapist, and workers such as the Gray Ladies. The modern hospital should omit no facet of the rehabilitation program. Too often, there is no interest in training the resident personnel in these fields. Many physicians enter practice with a keen interest in their own specialty, but an abysmal lack of knowledge about related specialties. Any orthopedist treating geriatric patients must have the wide knowledge of the internist and in addition must be somewhat of a humanist.

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ELECTROCARDIOGRAPHIC MANIFESTATIONS OF RIGHT VENTRICULAR HYPERTROPHY DUE TO RHEUMATIC MITRO-TRICUSPID HEART DISEASE

MYRON R. SCHOENFELD, M.A., M.D.*

The New York Cardiac Center, Yonkers, New York

Frank right ventricular hypertrophy often cannot be detected electrocardiographically, particularly in patients with acquired heart disease. Some of these cases may be caused by a counter-balancing left ventricular hypertrophy or other complicating factors but, even so, the impression remains that the commonly accepted criteria for electrocardiographic diagnosis are deficient.

Ideally, a satisfactory set of criteria would detect even the mildest case of right ventricular hypertrophy; at the very least, it should identify the severe cases. Amongst the severest cases of right ventricular hypertrophy in acquired heart disease are those due to rheumatic mitral stenosis with tricuspid insufficiency. There are only a few reports on the electrocardiographic findings in such patients (1–4), and in only one of these reports are the electrocardiographic details presented (1). We therefore undertook a study to test the adequacy of the criteria for right ventricular hypertrophy and right ventricular diastolic overload in a group of patients with rheumatic mitro-tricuspid disease. The results of this study are presented here.

MATERIALS AND METHODS

All of the 11 patients had clinical and radiographic evidence of mitral stenosis and tricuspid insufficiency. In addition, all were thought to have mitral insufficiency, and 5 also had aortic and/or pulmonic valvular disease. The diagnosis of tricuspid insufficiency was based on the clinical criteria of severe congestive heart failure with marked peripheral edema and ascites, systolic pulsations of the liver and neck veins, a pansystolic murmur in the tricuspid area accentuated by inspiration, relative freedom from orthopnea, cyanosis, and right ventricular hypertrophy on x-ray examination.

The conventional twelve-lead electrocardiograms on these 11 patients were subjected to analysis. Emphasis was placed on the criteria for right ventricular hypertrophy. Since all of the patients were receiving digitalis, the ST and T changes did not necessarily reflect myocardial disease; hence these changes were not included in the study.

In the discussion that follows, the term QRS will be used in a generic sense to describe the electrocardiographic deflection caused by ventricular depolarization, whatever the pattern. Capital letters are used for each of the component waves of the QRS, regardless of their absolute or relative sizes.

RESULTS

Rhythm. Ten of the 11 patients had atrial fibrillation; 1 had normal sinus rhythm with normal P waves.

Standard bipolar limb leads. Seven of the patients had right axis deviation, and

* Correspondence should be addressed to the author at 11 Bronx River Rd., Yonkers, New York.

in 5 the deviation was marked (greater than +110°). Three patients showed a normal electrical axis, and 1 a left axis deviation. The combination of marked right axis deviation and a Q wave in V_1, described by Cabrera and Estandia as highly characteristic of tricuspid insufficiency (1), occurred only twice. The $S_1S_2S_3$ syndrome (5) was seen in only 2 of the 11 cases. The S_1Q_3 pattern was not seen; neither was the Katz-Wachtel sign (6) of large biphasic QRS complexes in the three standard leads. The QRS was widened beyond 0.08 second in only 1 instance—to 0.13 second.

Lead aVR: Lead aVR showed a QR pattern in 8 patients, a QS pattern in 2, and an R pattern in 1 patient. None of the 11 had an R wave taller than 3 mm., and the height of the entire QRS complex exceeded 6 mm. in only 2 cases. When an R wave was seen, it tended to be wide and slurred rather than tall, varying between 0.03 and 0.08 second. The R/Q ratio exceeded unity in only 2 patients and equalled unity in 4 patients.

Right precordial leads. The RSR′ pattern in V_1 was noted in 3 cases, the QR pattern in 2, the RS pattern in 5 and the R pattern in 1 case. The amplitude of the QRS complex in V_1 tended to be small; in 7 cases it was less than 5 mm., and in 10 cases less than 10 mm. in height. The tallest positive deflection in V_1 (R or R′) was 4 mm. or less in 8 cases, and between 7 and 11 mm. in 3 cases. The R/S ratio in V_1 exceeded unity in only 6 patients. The sum of the R in V_1 plus the S

TABLE 1

Electrocardiographic characteristics of the QRS Complex in the Diagnosis of Right Ventricular Hypertrophy

Electrocardiographic signs	No. of Patients*
R of AVR 0.03 sec. or more in duration	11
Prominent S waves V_{2-5}	10
QRS in AVR 6 mm. or less in amplitude	9
S of V_6 0.04 sec. or more in duration	8
Absence of Q wave in V_6	7
S of V_6 4 mm. or more in depth	7
QRS in V_1 5 mm. or less in amplitude	7
Right axis deviation	7
Time of onset of intrinsicoid deflection in V_1 greater than 0.03 sec.	7
Time of onset of intrinsicoid deflection in V_1 greater than in V_6	6
R of V_1 plus S of V_6 10 mm. or more	6
R/S ratio in V_1 greater than 1	6
Right axis deviation of 110° or more	5
R or R′ in V_1 7 mm. or more in height	3
RSR′ pattern in V_1	3
Q wave in V_1	2
R/S ratio in AVR greater than 1	2
$S_1S_2S_3$ syndrome	2
Marked right axis deviation with Q in V_1	2
QRS in V_1 wider than 0.10 sec.	1
R wave in AVR 5 mm. or more in height	0

* The number among the 11 patients in our series who showed these features.

of V_6 exceeded 10 mm. in only 6 instances. The onset of the intrinsicoid deflection in V_1 was 0.04 to 0.10 second in 7 cases and 0.02 or less in 4 cases.

Left precordial leads. The depolarization pattern in V_6 was RS in 6 cases, QRS in 3, R in 1, and QR in 1 case. The R wave was 40 mm. in 1 case, 42 mm. in 1, and 13 mm. or less in the remaining 9 cases. Except in 2 patients with tall R deflections in V_6, the sum of the S of V_1 and the R of V_6 was less than 20. The time of onset of the intrinsicoid deflection in V_6 was 0.05 second or less in all cases; it was shorter than the time of onset in V_1 in 6, longer in 4, and equal in 1 case. S waves in V_6 occurred in 9 patients; they were 4 to 7 mm. in depth in 7, and 0 to 2 mm. in 4 patients. The S waves were 0.04 to 0.08 second in duration in 8 cases, and 0 to 0.01 second in 3 cases. The R/S ratio in V_6 was less than 1 in only 4 patients. Prominent S waves from V_2 through V_5 were noted in 10 of the 11 cases. The large biphasic QRS complexes in V_2-V_5 that are allegedly suggestive of biventricular hypertrophy (7) were seen in only 1 case.

DISCUSSION

All 11 patients manifested expansile systolic pulsations of the liver. This sign indicates a regurgitant flow of at least 3.5 liters per minute (8), and it hallmarks only the severest cases of tricuspid incompetence (9). Therefore one would expect a high incidence of marked right ventricular hypertrophy in such cases. Yet, on the basis of the commonly accepted electrocardiographic criteria, the incidence of right ventricular hypertrophy in our series of cases was unpredictably low (Table 1). In our experience, signs of greater usefulness are wide R waves in aVR, deep and wide S waves in V_6, prominent S waves across the mid-precordium, QRS complexes of small amplitude in aVR and V_1, and the absence of Q waves in the left precordial leads. These signs tend to persist even in the presence of left ventricular hypertrophy.

The right ventricular diastolic overload pattern of Cabrera and Monroy (10) was noted 4 times. A wide QRS in V_1 with an RSR′ configuration (*i.e.*, right bundle-branch block) was seen in only 1 of the 11 cases, but an RSR′ pattern with a normal QRS duration and a delayed time of onset of the intrinsicoid deflection was seen in 3 cases. It would thus appear that the electrocardiographic concept of right ventricular diastolic overload has only limited applicability in acquired heart disease—a conclusion in agreement with those of other workers (11).

SUMMARY

Electrocardiographic features are described for 11 clinically diagnosed cases of severe tricuspid insufficiency due to rheumatic mitral stenosis and insufficiency, with or without aortic or pulmonic valve disease.

Although almost all of the commonly accepted electrocardiographic signs of right ventricular hypertrophy were present in this series, certain other signs occurred more frequently, namely, a broad R wave in aVR, prominent S waves in V_2 through V_5, a small amplitude of the QRS in aVR and V_1, a deep broad S wave in V_6, and absence of Q waves in V_6. The right ventricular diastolic

overload pattern was seen only 4 times. Atrial fibrillation was noted in 10 of the 11 cases.

Acknowledgment

The author wishes to express his appreciation to Dr. William J. Welch, Dr. Coenraad Westermann, and Dr. Frank Seixas of the Medical Service of the New York Cardiac Cnter for their cooperation in making the records of their patients available.

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ORNITHOGALUM UMBELLATUM IN THE TREATMENT OF CONGESTIVE HEART FAILURE: PROGRESS REPORT

ARTHUR VOGELSANG, M.D.*

London, Ontario, Canada

In a preliminary report (1) the author mentioned the work of Waud (2) and Waud and Boyd (3) who prepared an extract from the bulbs of *Ornithogalum umbellatum* (Star of Bethlehem) and demonstrated its positive inotropic effect upon both the intact and isolated hypotonic animal heart. That report also mentioned a few clinical cases of congestive heart failure in which an enteric-coated pill made from this extract was used successfully.

In the six years which have passed since this preliminary report the clinical activity has been tested in 44 cases of progressive cardiac failure.

The pharmaceutical chemists have not been idle during these years. I have permission to quote Dr. G. R. Paterson (4), Associate Professor of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Toronto, as follows:

"Duncan (5) established that there was present in extracts of *Ornithogalum umbellatum* bulbs a rhamnoside-glycoside. The principle was a steroid of the digitalis type; possessing an α-β unsaturated five-membered lactone ring. Ultra-violet absorption studies indicated also a substance possessing a C_{16} hydroxyl group in the aglycone portion.

"Subsequent research by Kofoed (6) established the presence of at least nine glycosides in extracts of the bulbs. One glycoside was isolated in crystalline form and identified as convallatoxin. A second glycoside was partially identified by cleavage—giving strophanthidin and two sugars, one of which was glucose. Another crystalline compound was isolated but not identified. Also isolated was an amorphous glycoside lacking a lactone ring. The presence of a 2-desoxy sugar was indicated in this structure."

METHODS

This material was used only in cases of congestive failure which were becoming worse in spite of diuretics, digitalis and all other medication as well as a low-sodium diet. The digitalis preparation (digitoxin) was stopped, and *Ornithogalum umbellatum* tablets started in a dosage of two to four each day. The ancillary therapeutic measures were continued. In some of the successful cases it became necessary later to re-introduce very small doses of digitalis (less than 0.05 mg. daily) for purposes of slowing the heart rate.

RESULTS

On about the third day of medication an improvement in compensation was noted, with a decrease in pulmonary congestion and peripheral edema (when

* *Address:* 305 Oxford Street, London, Ontario, Canada.

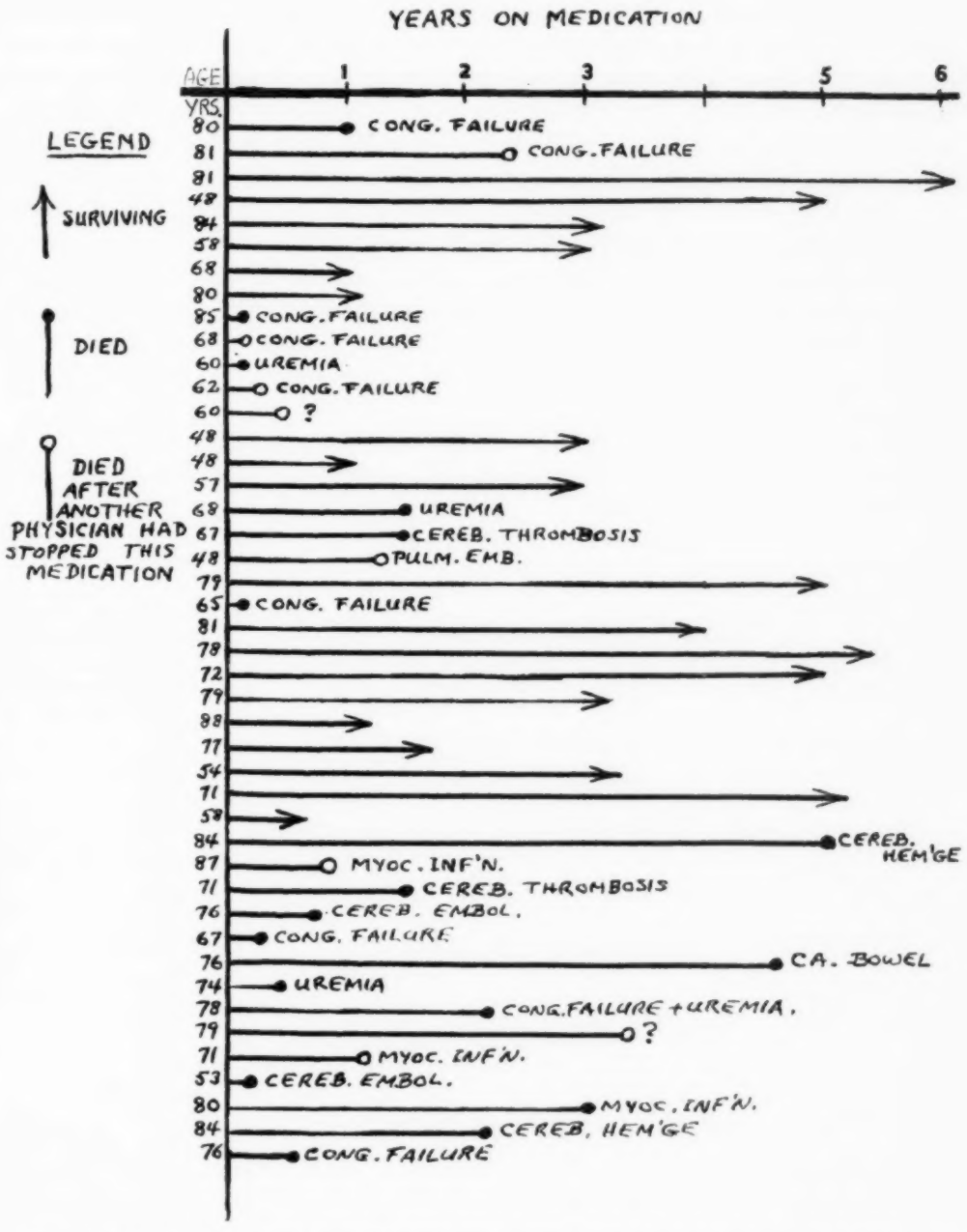

FIG. 1. Length of survival in 44 patients with congestive heart failure treated with *Ornithogalum umbellatum* tablets. The causes of death are indicated in the 25 patients who died. Thirty patients survived more than one year, and 6 survived between five and six years.

the latter had been present), accompanied by a relative diuresis. Cyanosis, when present, was relieved. In the ensuing weeks the dosage of diuretic was reduced or discontinued.

The results in the 44 cases are summarized in Figure 1. In this graph, the

age of the patient at the time treatment was started is noted at the beginning of each line. The duration of survival is denoted by the length of the line for each patient. The arrows indicate patients who are at present alive and doing well; the large black dots denote deaths from the causes indicated; and the circles denote deaths after the medication was discontinued on other medical advice. In 2 cases the medication did not arrest the process in any degree and the patients soon died. Another patient died in two weeks, of uremia. All the other patients were able to go about cautiously outside without symptoms. Some were able to go South for the winter or to take trips to other cities. None was confined to bed. One died in four months and another in seven months of congestive failure. Of the 30 who survived more than one year, only 1 died of congestive failure, and that was associated with uremia. Other survival and mortality data are as follows:

Duration of Medication (years)	Number of Patients
Living	
Over 6	1
5–6	5
4–5	1
3–4	5
2–3	1
1–2	5
Dead	
5–6	1
4–5	1
3–4	2
2–3	3
1–2	6
6 mos.–1	3
Survival (all 44 Patients)	
Over 1	31 (71%)
Over 2	20 (46%)
Over 3	16 (36%)
Over 4	9 (20%)
Over 5	7 (16%)
Over 6	1 (2%)

The average age for the 6 patients who died of cerebrovascular accidents was 74 years, and for the 3 cases who died of acute myocardial infarction, 81 years; in 2 of these the medication had been stopped. It does not seem likely that the medication caused either the cerebrovascular accidents or the myocardial infarction.

DISCUSSION

These experiences with 44 cases of congestive failure indicate that an extract prepared after the method of Waud (2) from *Ornithogalum umbellatum* (Star of Bethlehem) bulbs and used in an enteric form will often improve cardiac function and restore compensation in about three days.

Since no slowing of the heart rate was noted, and since Waud and Boyd (3) obtained results with isolated as well as intact hearts, it is probable that the action is not through the vagus but directly on the heart muscle.

Chemical analysis reveals the presence of 9 different glycosides. Since these have not all been identified it is impossible to state at this time which glycoside, or combination of glycosides, accounts for the clinical action. Mathematically there would appear to be 511 possible combinations.

Speculation about the possible effects of this medication on pulmonary, peripheral or renal vessels is idle. The simplest explanation—the one which best explains the recovery from congestive failure—is that of increased cardiac output.

All patients in whom this medication was stopped died within three weeks.

SUMMARY

Forty-four cases of progressive congestive failure were treated by substituting an *Ornithogalum umbellatum* preparation for digitalis. In at least three-quarters of these cases the clinical improvement was significantly greater than could be expected.

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NEWS AND NOTICES

ARTERIOSCLEROSIS—THE CONCENTRATION CAMP DISEASE

More than 10,000 autopsies made during 1941–1945 in the Nazi concentration camp of Dachau showed that all prisoners, apart from those who died immediately after entering the camp, suffered from arteriosclerosis. This fact was disclosed by Prof. Dr. Frantisek Blaha of Prague at an international medical conference dealing with late effects of imprisonment and deportation, held in Liege (Belgium) recently by the International Federation of Resistance Fighters (F.I.R.).

Prof. Blaha, himself a prisoner at Dachau, worked in the camp hospital and carried out or studied all these autopsies. The examinations were made on all victims of the "medical experiments" of the Nazi doctors, from 1942 on all prisoners who died in the camp hospital, and from 1943 on all who died from exhaustion, starvation, accidents, disease or other causes. In addition, random tests were carried out on victims of mass executions or severe epidemics.

The actual cause of death was rarely arteriosclerosis, and the living prisoner never complained about symptoms typical for this disease. Nevertheless, sclerotic deformations were observed again and again, particularly on the heart valves, the coronary vessels, the aorta and the brain arteries. These arteriosclerotic lesions were severer than would have been expected according to the age of the deceased and were all the more pronounced the longer camp detention had lasted.

Not "sins of prosperity"

Life in the camps was by necessity completely free of many influences supposed to promote arteriosclerosis. The prisoners had no opportunity at all for drinking even the smallest amount of alcohol or for smoking. They certainly did not eat animal fats or proteins in excessive quantities. On the contrary, for years they did not consume a single gram of such foodstuffs. Vegetable proteins were also very rare in the camp diet, which mainly consisted of carbohydrates with a daily caloric value of about 1,000 during the first years, deteriorating to 500 calories towards the end of the war. In addition, the prisoners spent most of their time doing hard physical work in the open air.

All these facts clearly show that arteriosclerosis is not necessarily provoked only by factors connected with the so-called "sins of prosperity" but is also caused, maybe to a greater extent, by the entirely different conditions of the Nazi concentration camps. According to many participants of the conference at Liege, the disease is a direct consequence of the intense physical and mental stress to which the prisoners were subjected. That extreme stress can cause arteriosclerosis was demonstrated by animal experiments, and there are fairly clear ideas as to the hormonal mechanisms which transform extreme nervous stress into arteriosclerosis. (A detailed study on this subject is given in the book

"Premature Ageing and its Treatment, Based on Observations Made on Former Concentration camp Internees and Deportees" by Dr. L. F. Fichez and Dr. A. Klotz, published in French and German by the FIR, Vienna II, Castellezgasse 35. An English translation is in preparation.)

Absence of typical symptoms

There is every reason to assume that those former concentration camp prisoners who survived are also afflicted with arteriosclerosis even though this could not generally be ascertained when examining the prisoners clinically immediately after liberation. Camp arteriosclerosis has special features, as Prof. Blaha pointed out. Many typical symptoms generally associated with the disease, such as hypertension (high blood pressure), do not appear. Nevertheless, the ailment exists and has since grown worse in many instances, particularly in persons who took responsible work soon after liberation which also involved nervous stress, although of quite a different kind.

There is therefore no justification for many medical experts to ascribe arteriosclerosis in former internees only to old age and post-war influences, by referring to the examination results immediately after liberation in which there is no word about arteriosclerosis. The material, so tragically large, presented by Prof. Blaha leaves no room to doubt that the time spent in concentration camps at least decisively *contributed* to the development of arteriosclerotic afflictions in former concentration camp prisoners which may cause premature inability to work today. These facts should be duly considered when deciding on pensions and similar claims.

CALL FOR PAPERS

The 19th Annual Meeting of the American Geriatrics Society will be held at the Palmer House, Chicago, Illinois, on Monday, Tuesday and Wednesday, *June 18, 19 and 20, 1962.*

Abstracts of papers for this meeting should be submitted to the Chairman of the Program Committee for consideration. Abstracts should be submitted in duplicate, double spaced, and include the title, author(s), etc. The text of the abstracts should be a complete synopsis so that the reviewer may adequately evaluate the complete work. The author should indicate at the end of the abstract whether he would present lantern slides or moving pictures (size; sound or silent). Abstracts are limited to 250 words.

Each speaker may use 20 minutes for his paper, followed by a 5-minute discussion period. Moderators will be asked to enforce the 25-minute period. Speakers are urged to check the length of their presentation.

Before January 1, 1962 send abstracts to: Program Chairman, American Geriatrics Society, 10 Columbus Circle, New York 19, N.Y.

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Published monthly by The Williams & Wilkins Co., 428 E. Preston St., Baltimore 2, Md., U.S.A.
Subscription price $10.00 per volume, single issue $1.25
Second class postage paid at Baltimore, Md.

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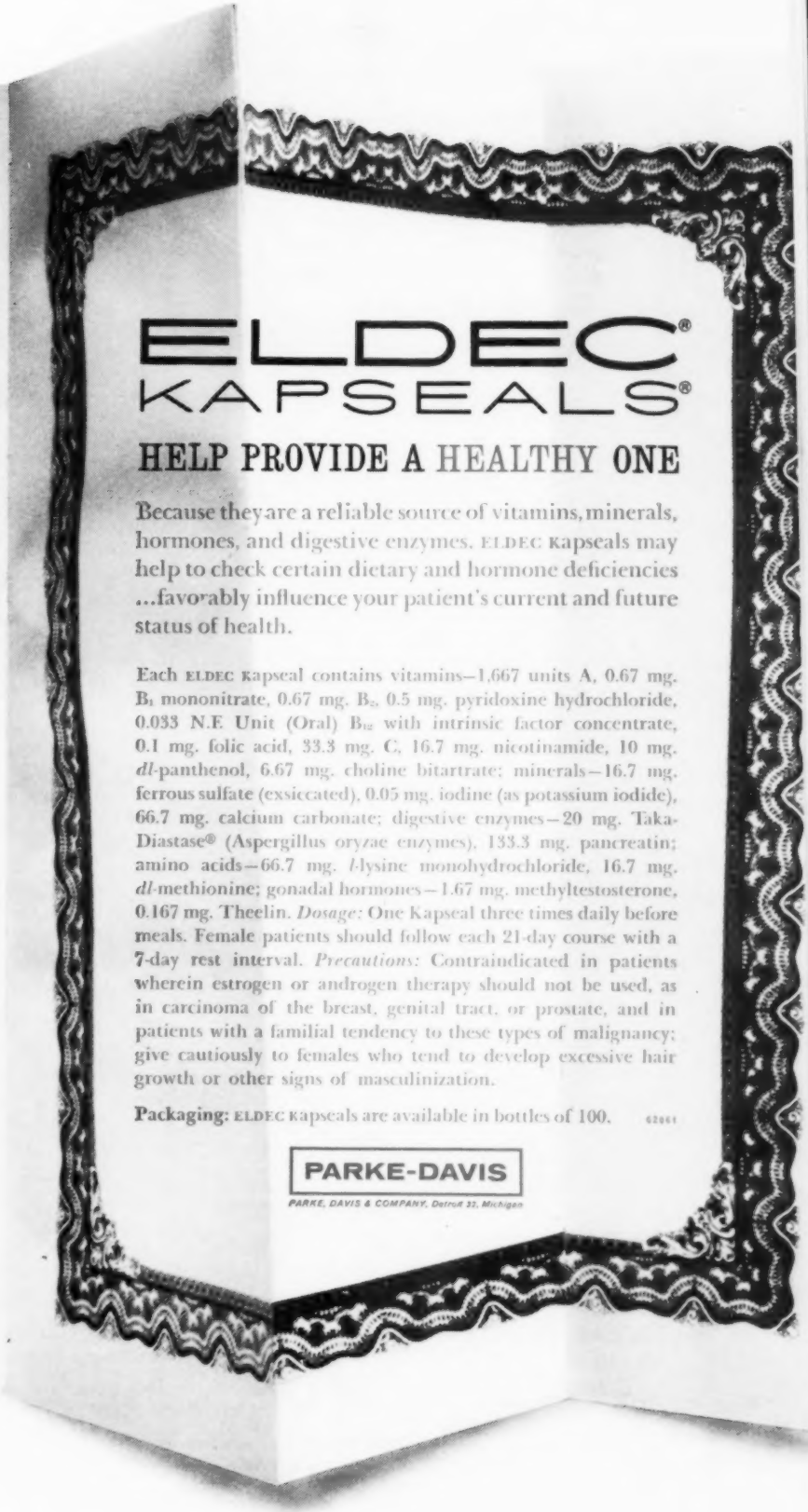
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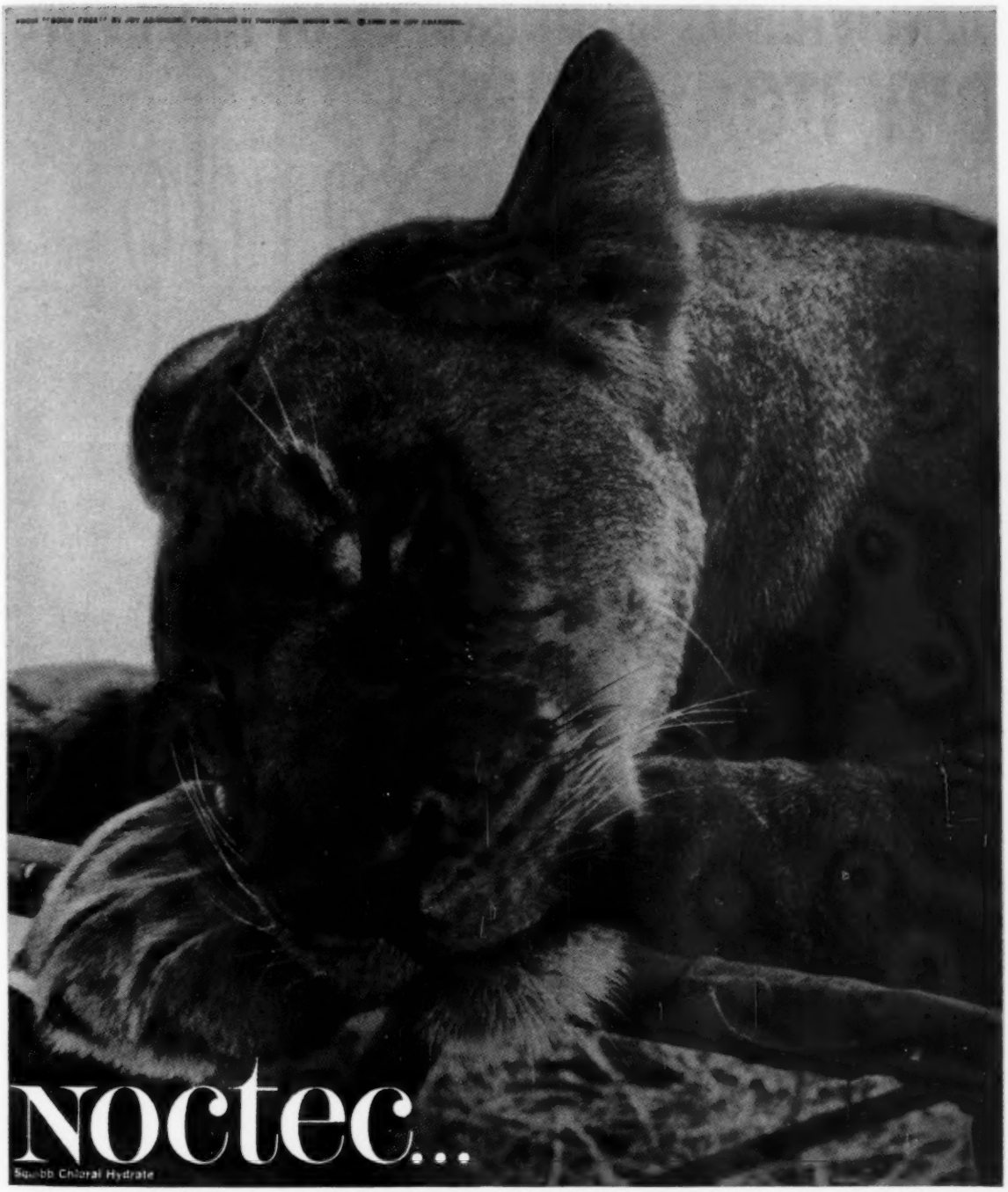

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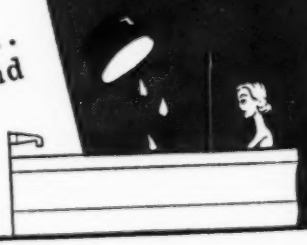

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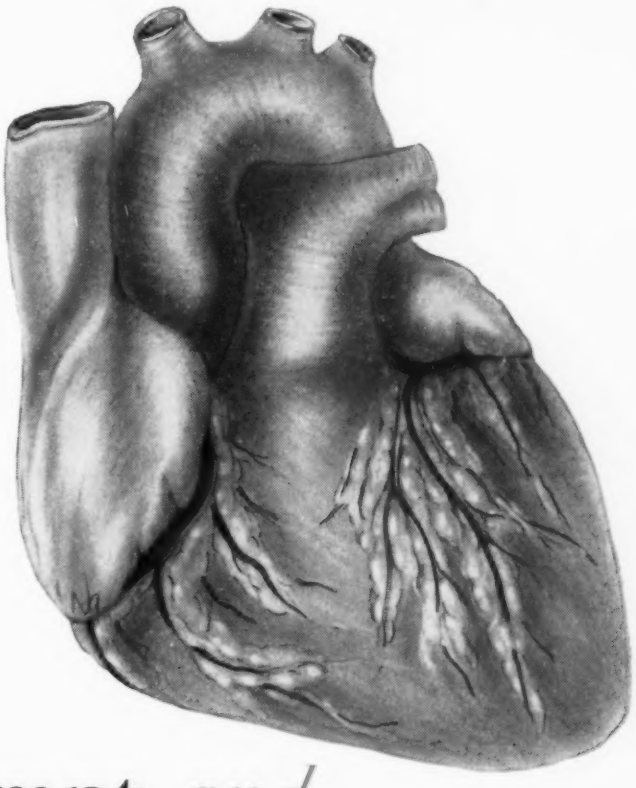

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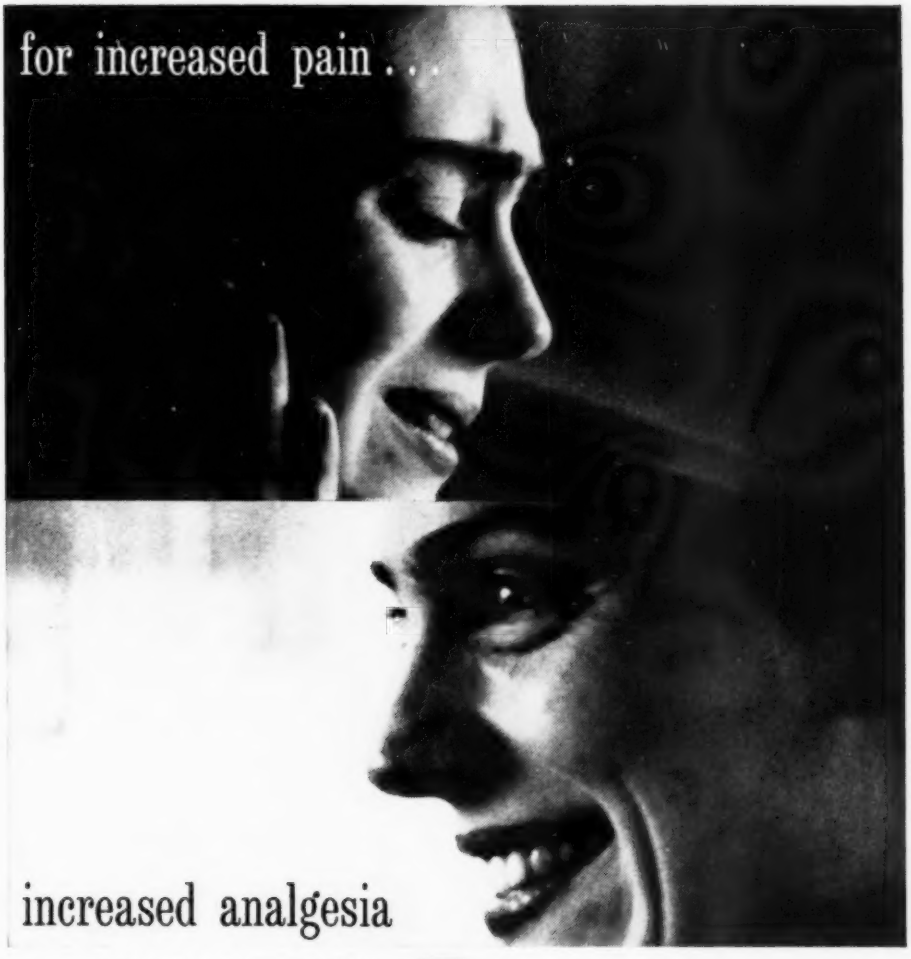

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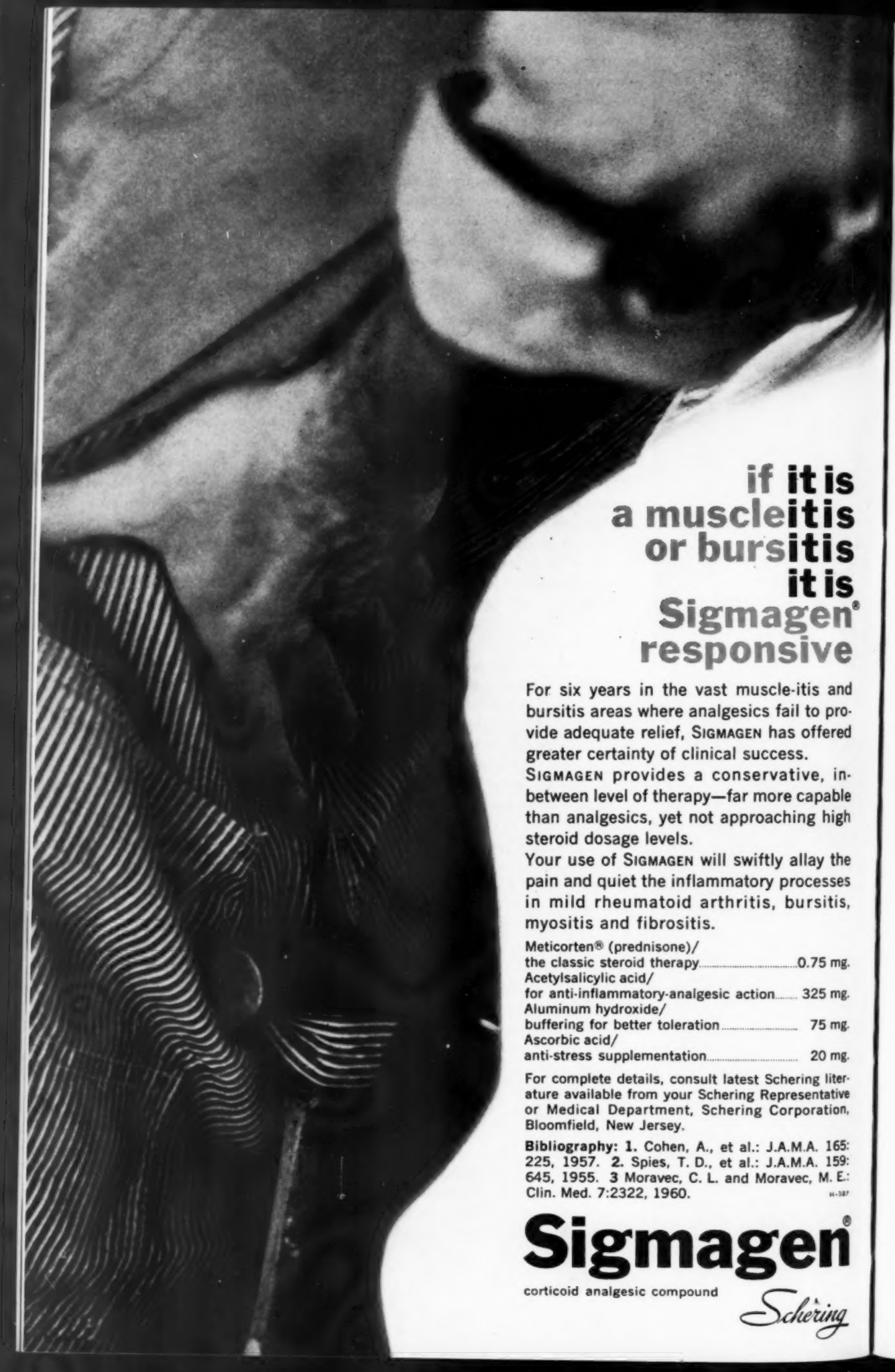

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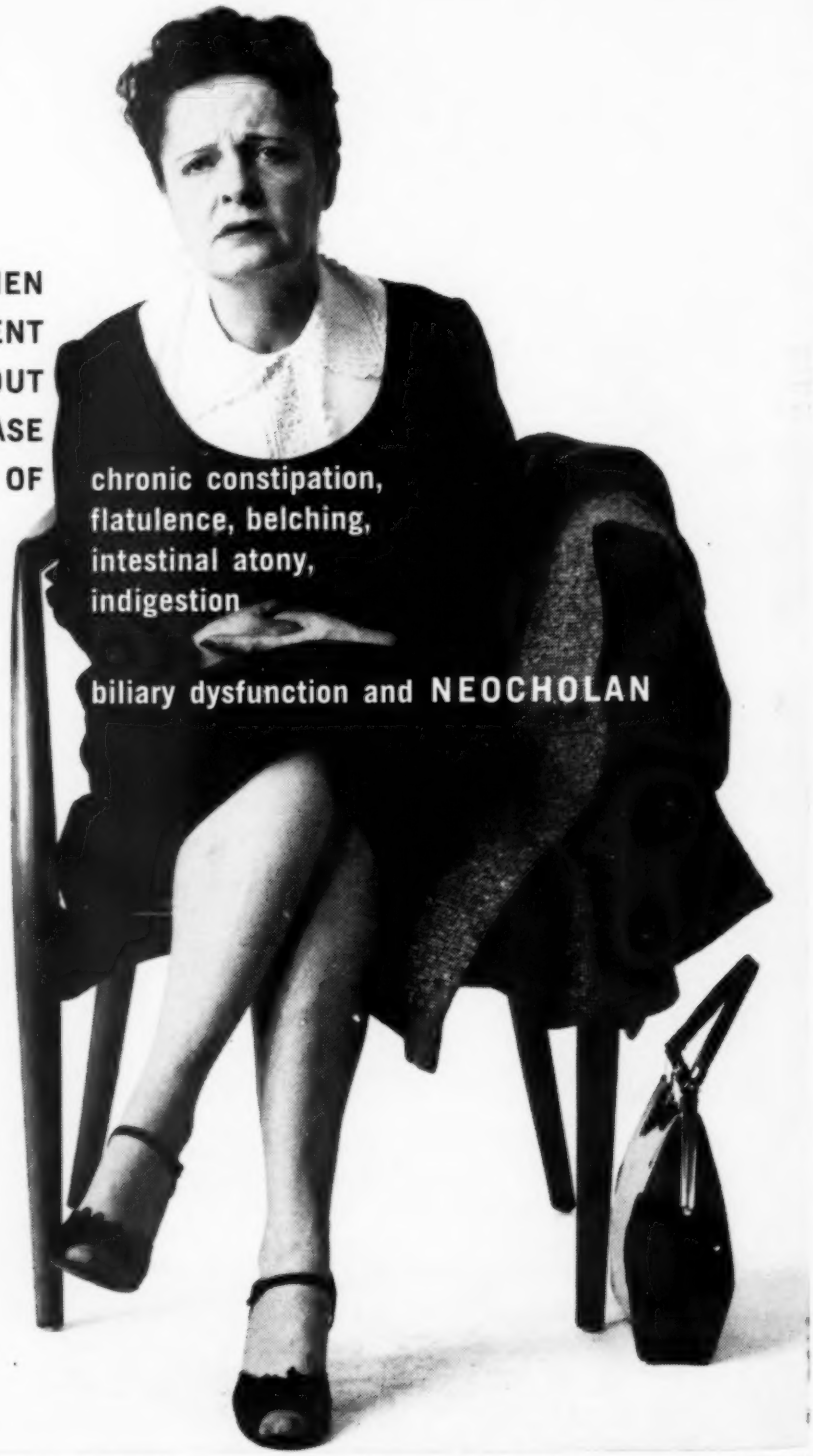

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1. Youmans, J. B.: Am. J. Med. 25:659 (Nov.) 1958. 2. Overholser, W., and Fong, T. C. C. in Stieglitz, E. J.: Geriatric Medicine, 3rd edition, J. B. Lippincott, Philadelphia, 1954, p. 264.

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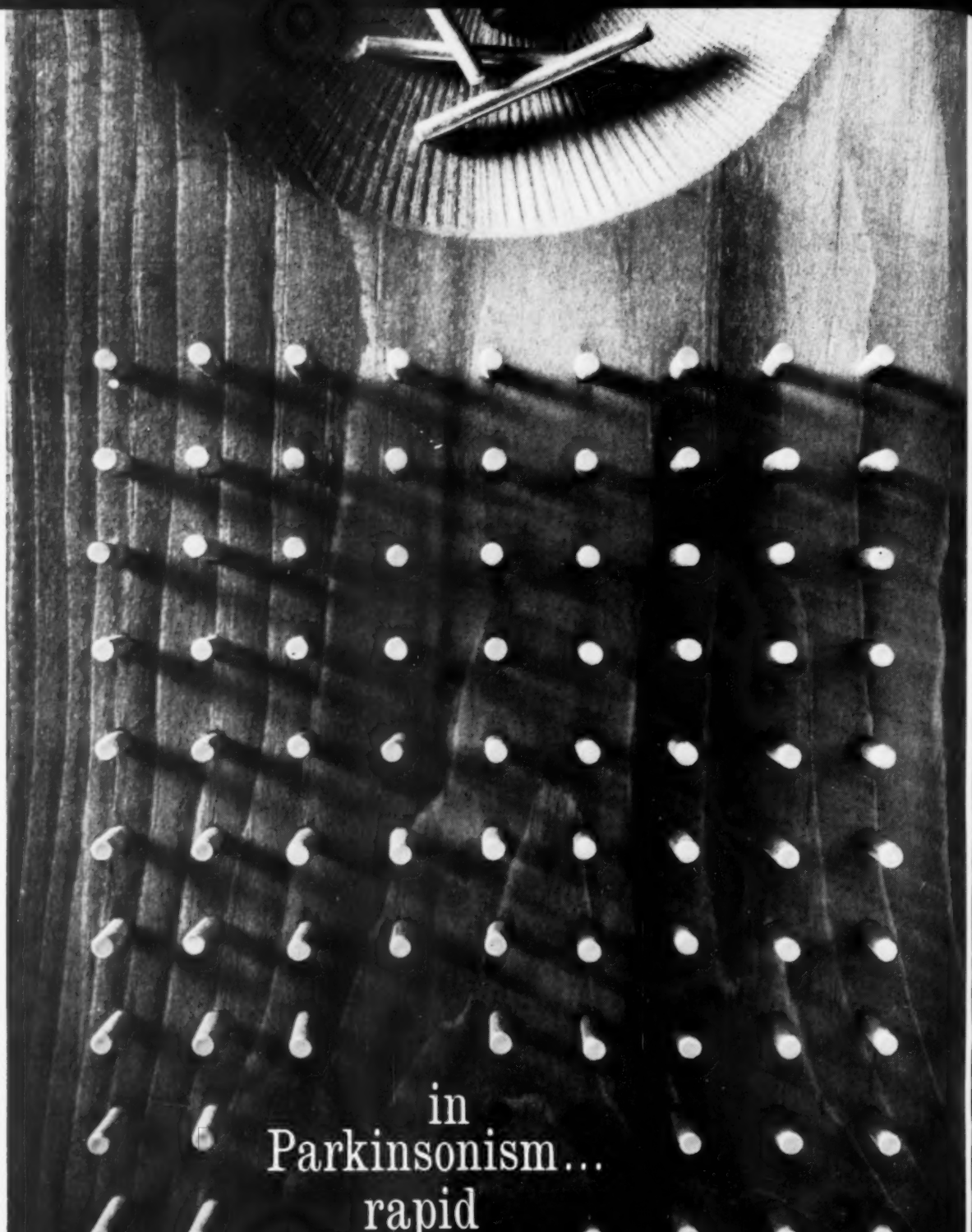

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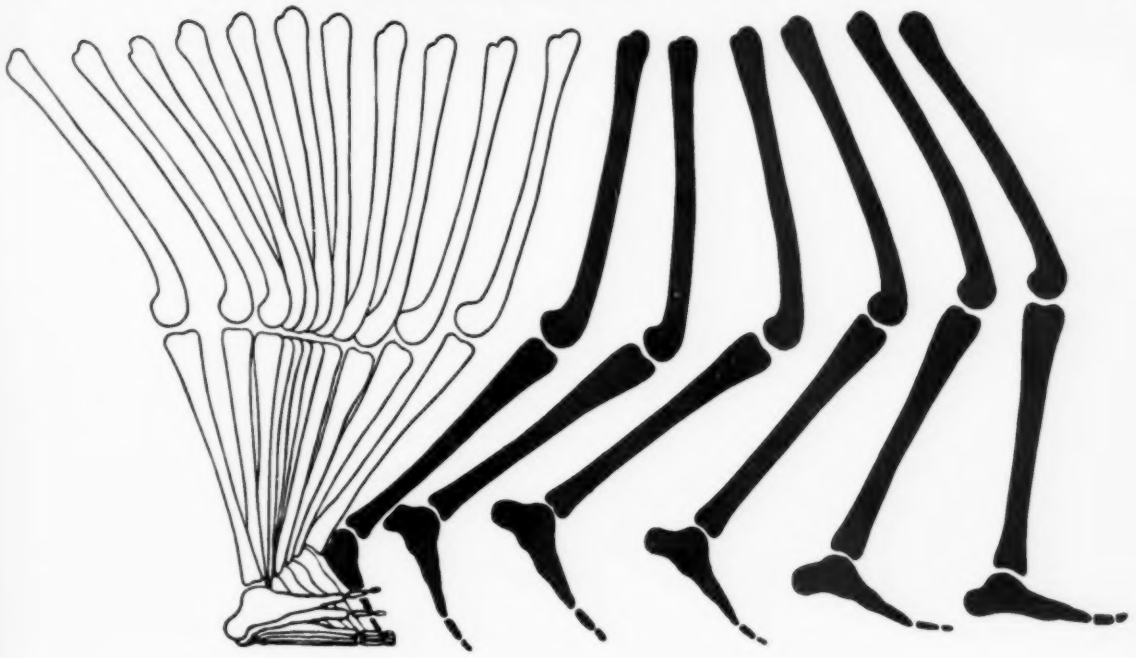

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Myristyl-gamma-picolinium chloride	0.19 mg.
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Supplied: 1 cc. and 5 cc. vials

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1. Norcross, B. M., and Winter, J. A.: Methylprednisolone acetate: a single preparation suitable for both intra-articular and systemic use, New York J. Med. *61*:552 (Feb. 15) 1961.

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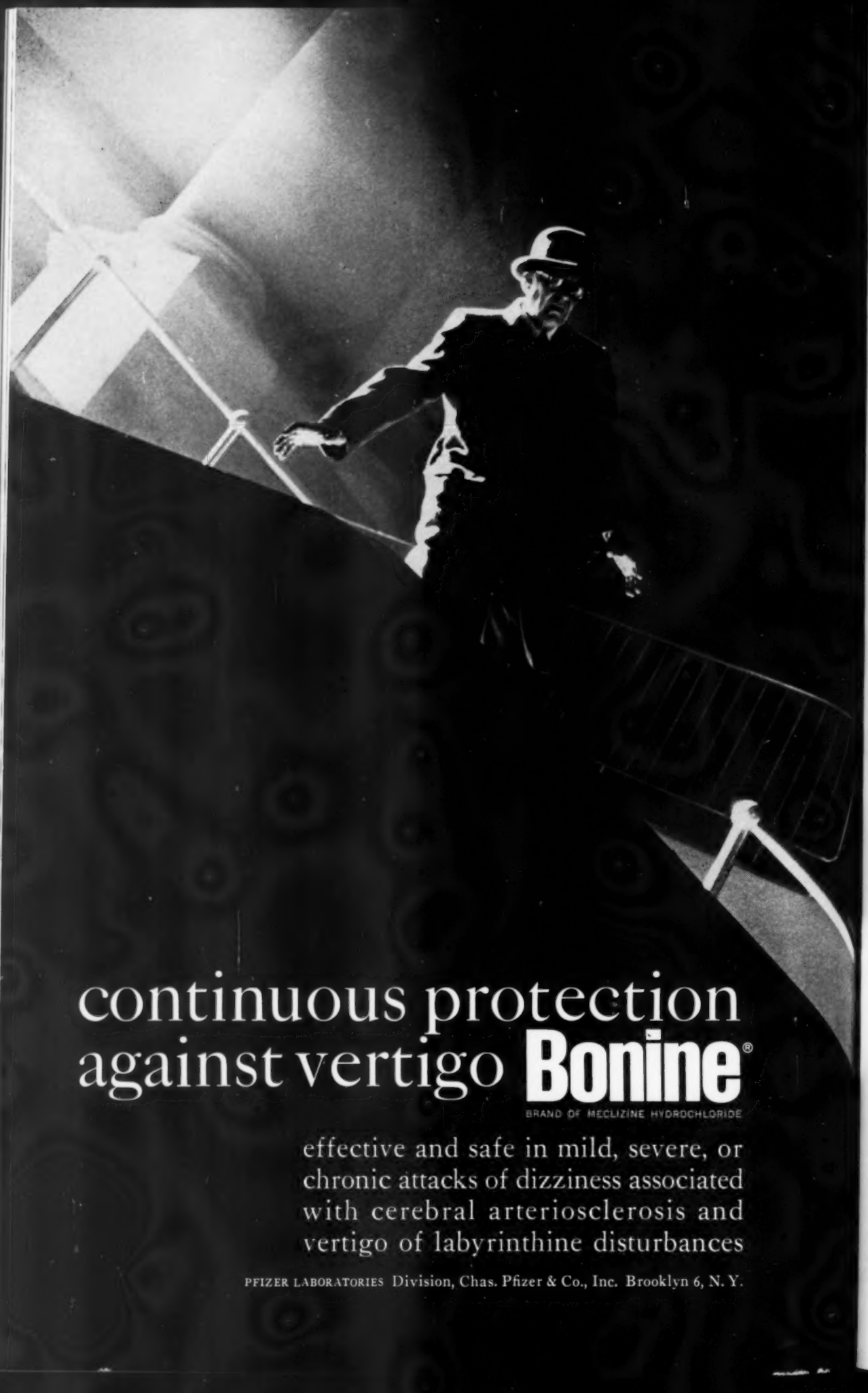

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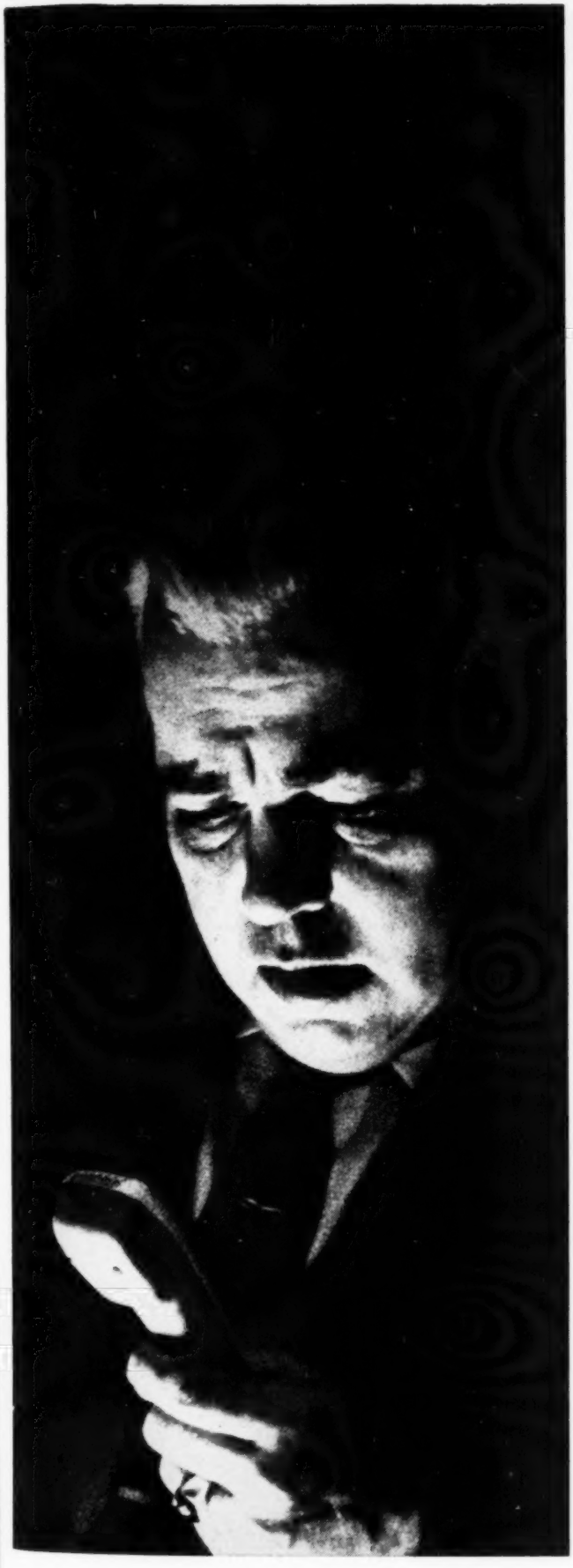

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